PB80-213879

Coal Tar, Creosote, and Coal Tar Neutral Oil Position Document 1

(U.S.) Environmental Protection Agency
Arlington, VA

18 Oct 78

U.S. Department of Commerce
National Technical Information Service
NTIS

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO. EPA/SPRD-80/82	2.	3. Recipient's Accession No. PB 80 213879

4. Title and Subtitle

Coal Tar, Creosote, and Coal Tar Neutral Oil: Position Document 1

5. Report Date

10/18/78

6.

7. Author(s)

8. Performing Organization Rept. No.

9. Performing Organization Name and Address

Special Pesticide Review Division
Environmental Protection Agency
Crystal Mall #2
Arlington, VA

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.

(C)

(G)

12. Sponsoring Organization Name and Address

Environmental Protection Agency
401 M. St. S.W.
Washington, D.C. 20460

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

Preliminary Risk Assessment: Examination of possible unreasonable risks associated with uses of pesticide and a gathering of all available information to determine whether or not this or any other risk does exist. Initiates literature search and evaluates risk data. Limited information on exposure to forecast extent of risk.

17. Document Analysis a. Descriptors

0504,0703,0606

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages
Unlimited	Unclassified	116
	20. Security Class (This Page)	22. Price
	Unclassified	

(See ANSI-Z39.18) See Instructions on Reverse

OPTIONAL FORM 272 (4-77)
(Formerly NTIS-35)
Department of Commerce

PB80-213879

COAL TAR, CREOSOTE, AND COAL TAR NEUTRAL OIL

POSITION DOCUMENT 1

Coal Tar and Coal Tar Products Working Group
Herman Gibb, Project Manager
U.S. Environmental Protection Agency

EPA/SPRD-80/82

REPRODUCED BY
NATIONAL TECHNICAL
INFORMATION SERVICE
U.S. DEPARTMENT OF COMMERCE
SPRINGFIELD, VA. 22161

TABLE OF CONTENTS

Pages

I. Background ... 1
  A. Chemical and Physical Characteristics ... 1
  B. Registered Uses, Production, and Supply ... 3
    1. Uses ... 3
    2. Production and Supply ... 3
  C. Fate in the Physical Environment ... 6
    1. Vapor Loss From Land Use ... 7
    2. Loss in a Marine Environment ... 7
    3. Loss in a Freshwater Environment ... 9
  D. Fate in the Biological Environment ... 9
    1. Microbial Degradation ... 9
    2. Bioaccumulation ... 10
    3. Effect on Freshwater Organisms ... 11
  E. Regulatory History ... 11

II. Summary of Scientific Evidence Relating to Rebuttable Presumption.. 12
  A. Oncogenicity ... 12
    1. Summary Table of Coal Tar, Creosote, and Coal Tar Neutral Oil Studies ... 13
    2. Coal Tar ... 19
      a. Case Reports of Skin Cancer of Workers ... 19
      b. Animal Studies ... 21
    3. Creosote ... 52
      a. Case Reports of Skin Cancer in Workers ... 52
      b. Animal Studies ... 55
    4. Coal Tar Neutral Oil ... 69

Pages

5. Conclusion.. 73

a. Coal Tar.. 73
b. Creosote.. 74
c. Coal Tar Neutral Oil............................ 75

B. Mutagenicity.. 75

C. Exposure.. 85

III. Other Adverse Effects............................. 96

A. General... 96

B. Skin and Eye Irritation............................. 97

C. Toxicity to Livestock............................... 99

D. Fetotoxicity.. 102

I. Background

A. Chemical and Physical Characteristics

Coal tar is produced by the carbonization, also called coking, of coal. Creosote and neutral oils are products of coal tar. Although creosote and neutral oil may be distilled from sources other than coal, the terms "creosote" and neutral oil" in this document will refer to distillates of coal tar. Coal tar is described in the Condensed Chemical Dictionary (Hawley, 1977) as:

> A black, viscous liquid (or semi-solid), naphthalene-like odor; sharp burning taste; obtained by the destructive distillation of bituminous coal, as in coke ovens; 1 ton of coal yields 8.8 gallons of coal tar. Combustible. Specific gravity 1.18-1.23 (60/60°F). Soluble in ether, benzene, carbon disulfide, chloroform; partially soluble in alcohol, acetone, methanol, and benzene; only slightly soluble in water.

Although it has other uses, the term creosote usually refers to that coal tar distillate which is used for wood preservation. Definitions of creosote vary, however.1/

1/ As a wood preservative, creosote is defined by the American Wood Preservers' Association (1976) as:

> A distillate derived from coal tar. As used in the wood preserving industry, creosote denotes a distillate of coal tar produced by the high temperature carbonization of bituminous coal. Creosote consists principally of liquid and solid aromatic hydrocarbons and contains some tar acids and tar bases; it is heavier than water and has a continuous boiling range beginning at about 200°C.

(continued on page 2)

Coal tar neutral oils are generally defined as a mixture of naphthalene, fluorene, anthracene, and other neutral hydrocarbons (Smale, 1977). Neutral hydrocarbons are those coal tar hydrocarbons other than coal tar acids (such as phenols, cresols, and cresylic acids), and coal tar bases (such as pyridines, quinolines, and acridines).

The actual constituents of coal tar, creosote, and the neutral oils are highly variable. They depend on the source of the coal used to produce the tar, the design and attendant operating conditions (temperature, coking time, gas collection systems) of the coke ovens, and in the case of the coal tar distillates the design and operating parameters of the still (e.g. the feed rate, temperature, and the blending of various tar distillate fractions) (Leach and Weinert, 1976).

Over three hundred compounds have been positively identified in coal tar. It is estimated that as many as ten thousand compounds may

---

1/ (continued from page 1)

The Condensed Chemical Dictionary (Hawley, 1977) defines cresosote as:

> A yellowish to dark brown, oily liquid; clear at 38°C or higher; naphthalenic odor; frequently contains substantial amounts of naphthalene and anthracene; distilling range 200-400°C; flash point 165°F (closed cup); soluble in alcohol, benzene, and toluene; immiscible with water. Combustible.

Von Rumker et al. (1975) defined creosote as a distillate of coal tar distilling in the temperature range 271-362°C, heavy creosote as distilling in the range of 285-395°C, and light creosote as distilling in the range of 238-291°C. Ross (1948) identified creosote oil as a distillate of coal tar distilling in the temperature range of 230-270°C.

exist, though many are present only in trace amounts (NIOSH, 1977). Because the composition of coal tar and coal tar products is known to vary, they are usually assayed and specified by their physical characteristics (including water content, specific gravity impurities, and fractional distillation curve). Using these physical characteristics, specifications for creosote used to pressure-treat wood have been established by the American Wood Preservers' Association, the American Society for Testing and Materials, and the United States General Services Administration (Appendix A). The American Wood Preservers' Association has also established specifications for creosote-coal tar solutions (Appendix B). About 98% of the creosote used for wood preservation in the United States is applied by pressure-treating methods (American Wood Preserver's Institute, 1977). Pressure-treating forces creosote to penetrate deeply into the wood.

B. Registered Uses, Production, and Supply

1. Uses

The largest pesticidal coal tar and creosote use is as a wood preservative. Coal tar is also used as an insect repellent, an acaricide, and a crow repellent. Creosote's other pesticidal uses are as an herbicide, an insecticide, an acaricide, an arachnicide, a fungicide, a tree dressing, a disinfectant, and a horse repellent. Coal tar neutral oil is registered as a disinfectant, a larvicide, an insecticide, a wood preservative, an arachnicide, an acaricide, and a fungicide. Specific uses and sites are given in Table 1.

2. Production and Supply

Von Rumker et al. (1975) reported that in 1972, 1,150 million

TABLE 1

USES AND SITES FOR COAL TAR, CREOSOTE, AND COAL TAR NEUTRAL OIL (Cummings, 1977)

Product	Use	Site
Coal Tar	Preservative	Wood
	Insect Repellent	Human Skin (Except Forehead)
	Acaricide	Dogs
	Crow Repellent	Seed Corn
Creosote	Preservative	Wood
	Insecticide (screwworm)	Horses and Mules
	Acaricide (mites)	Poultry Houses
	Arachnicide (ticks)	Poultry Houses
	Herbicide	Along Roads, Highways, and Fences Lawns; Flower Beds
	Fungicide	Rope, Canvas, Tarpaulins, Tree Wounds
	Tree Dressing	Certain Insects, Worms, Moths and Borers
	Horse Repellent	Wood Stalls, Mangers, Gates, Fenc Rails, Posts, Trees, Trailer Side
	Disinfectant	Outhouses, Water Closets, Garbage Cans, Feeding and Watering Equipm
Coal Neutral Oil	Preservative	Wood
	Arachnicide (ticks)	Hog Houses; Sheep Barns; Dog Kenn Horse Stables; Dogs.

TABLE 1
(continued)

USES AND SITES FOR COAL TAR, CREOSOTE, AND COAL TAR NEUTRAL OIL

Product	Use	Site
Coal Neutral Oil	Larvicide (mosquito)	Marshy Land; Stagnant Pools and Small Streams; Sewers; Drains; Small Non-fish Bearing Lakes and Ponds; Temporary Rain Pools; Rain Barrels; Clogged Gutters; Intermittently Flooded Areas; Tree Holes; Eaves; Canals and Ditches.
	Insecticide (srewworm)	Horses and Mules.
	Larvicide (gypsymoth)	Gypsy Moth Nests.
	Acaricide (mites)	Horses.
	Larvicide (fly)	Garbage Trucks.
	Insecticide (lice)	Horses; Dogs; Hog Houses; Sheep Barns; Dog Kennels; Horse Stables.
	Insecticide (fleas)	Hog Houses; Sheep Barns; Dog Kennels; Horse Stables; Dogs.
	Disinfectant	Soluble Cutting Oils for Machinery; Hog Houses; Sheep Barns; Dog Kennels; Horse Stables; Yards and Pens; Poultry Feeders; Waterers and Incubators; Boots; Animal Equipment and Utensils; Cellars; Sinks; Bed Pans; Washrooms; Garbage Cans and Pools; Homes; Factories; Offices; Schools; Public Buildings; Water Closets; Urinals; Spittoons; Sickroom Walls; Kitchens; Bathrooms; Lavatories; Woodwork and Floors; Wash Basins; Toilet Bowls and Seats; Livestock Trucks; Cotton Mills; Farrowing Equipment; Poultry and Meat Dressing Plants; Ships; Planes; Railroad Cars; Busses; Sick-room Thermometers; Dishes; Trays and Sputum Cups; Diaper Cans.
	Fungicide (ringworm)	Horses

pounds of creosote were used in the United States, of which 990 million pounds were domestically produced and 160 million pounds were imported. Of its total use, wood preservation accounted for 972 million pounds and fuel burning for about 178 million pounds. Fuller et al. (1977) reported that 96,266,000 gallons of creosote, approximately 843 million pounds, and 23,635,000 gallons of coal tar, approximately 238 million pounds, were used for wood preservation in 1975. Pesticide production data reported to the Environmental Protection Agency under Section 7 of FIFRA indicated that 34,847,384 pounds of coal tar, 366,839,110 pounds of creosote, and 2,019,951 pounds of coal tar neutral oil were formulated or blended for pesticidal use in 1975.

C. Fate in the Physical Environment

Little information is available in the literature regarding the environmental fate of coal tar and coal tar products used for purposes other than as wood preservatives. The following studies indicate that coal tar and creosote migrate to some extent from the treated wood into the surrounding environment. However, the impact of this migration is not known.

Leach and Weinert (1976) reviewed the literature on the loss of creosote from impregnated wood and found that the loss was dependent on many variables; among these are the kind of coal used to produce the coal tar, the kind of coke oven (temperature, coking time, and gas collection system) from which the coal tar is made, the distillation facilities and operating parameters (feed rate, temperature, and blend of various tar distillate fractions), the treatment and handling by the wood preservers (seasoning and incising of the wood; temperature, pressure, and time of treatment; and the after-treatment cooling period) and the situations under which the wood is used (surface of wood exposed, orientation of the creosoted wood with reference to the wood grain, and the exposure environment).

1. Vapor Loss

Stasse (1964) found that the creosote vapor loss was greater from seasoned poles than from green poles. Vapor loss is also related to the temperature distillate fractions of the creosote; the higher the temperature of the distillate fractions, the lower the vapor loss. Over a three-year period, low residue (residue, in this study, was defined as the portion of creosote distillate over 355°C) creosote was found to have a vapor loss of 27.5% and 15.2%, from the outer 2 inches of seasoned and green poles, respectively; high residue creosote was found to have a 10.3% and 4.4% vapor loss, respectively.

2. Loss in a Marine Environment

Bramhall and Cooper (1972) found that the creosote concentration in the treated zone of pilings of a 40-year-old wharf averaged 15 pounds per cubic foot (74% of the current minimum) in the outer 1.5 inches. Whether the substandard retention was due to the original treatment or to leaching could not be determined. Sweeney et al. (1958) found that creosote was lost from treated panels when wet due to the swelling of the wood fibers. Panels 5 x 1 1/2 x 1/8 inches were pressure-treated with creosote and exposed to flowing seawater at 25°C. Based on distillation analyses, approximately 30% of the creosote was lost in the first month of exposure. By the twelfth month, approximately 40% of the creosote was lost. The rapid initial loss was attributed to the initial hydration of the wood fibers resulting in mechanical loss. It would be difficult to determine the loss of creosote from marine pilings based on the loss from small panels. This work, however, does indicate that coal tar-creosote may be lost from marine pilings by mechanical means, if not by true leaching.

Miller (1977) found that the ability of Douglas fir marine piles to retain creosote in cool estuarine waters was directly related to the density of the wood. Of the three piles studied, one had a detectable loss of about 0.31 pounds of creosote per linear foot of immersed pile during the first year, 0.05 pounds/year the second year, 0.06 pounds/year the third year, 0.22 pounds/year the fourth year, and an average of 0.15 pounds/year each year for the last 4 years of the 8-year study. Thus, in the first year a pile with 30 feet of its length in water would lose about 9.3 pounds of creosote, a daily loss of about 11.6 grams. The speed of the water flowing past the pilings was about 2 feet per second during flood tide and about 0.8 feet per second during ebb tide; upstream tide volume between the mean lowest and the mean highest daily tides was 900 million cubic feet of water. Miller concluded that because of the velocity and the volume of the water flowing past the pilings, the creosote lost from the pilings was greatly diluted. Hochman (1967) found that about 20% of the creosote initially impregnated into wood is expelled in the marine environment during the first year as a result of wood hydration. Stasse (1967) found a creosote displacement loss of 21.7% from wood panels over a 6.5-year period in ocean water.

3. Loss in the Freshwater Environment

Kelso and Behr (1977) found that the greatest loss of creosote from round Southern Pine poles in fresh water occurred in the outer 0.5 inch zone where 48.1% of the creosote was depleted in 13 months. Overall losses for the 13-month period were 19.5%.

D. Fate in the Biological Environment

1. Microbial Degradation

Dean-Raymond and Bartha (1975) isolated six strains of bacteria from oil polluted estuarine water; all six grew on naphthalene, 2-methylnaphthalene, and 2-ethylnaphthalene. Phenanthrene and anthracene were metabolized by three of the six strains. Two of the six strains metabolized 1,5-dimethylnaphthalene and one strain metabolized 1-methylnaphthalene. Naphthalene, 2-methylnaphthalene, 2-ethylnaphthalene, 1-methylnaphthalene, and 1,5-dimethylnaphthalene have all been identified in creosote (National Research Council, 1945) (Lorenz and Gjovik, 1972).

Drisko and O'Neill (1966) found that the mixture of microorganisms present on creosoted pilings in the Port Hueneme, California harbor had the ability to metabolize creosote, causing loss of creosote from the pilings. Two of the aromatic hydrocarbons present in creosote - naphthalene and phenanthrene - were metabolized to a significant extent. Pseudomonas creosotensis, which was isolated from the mixture of microorganisms, utilized a number of neutral creosote constituents as a source of energy; conversely, acidic and basic creosote constituents inhibited its growth.

Hegner (1977) found that creosote in a soil to sand mixture (1:2) was decomposed by soil microorganisms. Fertilized soil plots were watered weekly for 22 weeks with the equivalent of one inch of rain per week. Analyses showed that the leachates degraded rapidly when creosote concentrations in the soil were 0.1% or lower. Higher concentrations of creosote can be degraded in the soil but at a much lower rate (Hepner, 1977).

Davies and Evans (1964) studied the metabolism of naphthalene by a Pseudomonas species. The ultimate metabolic products were salicylaldehyde and acetaldehyde.

2. Bioaccumulation

Dunn and Stich (1975) showed that mussels taken from creosoted pilings contained significantly more benzo[a]pyrene (B[a]P), a known carcinogen (IARC, 1976), than those growing on other surfaces. B[a]P has been identified as a constituent of creosote oil (Lijinsky et al., 1963). Mussels taken from the creosoted wood showed mean B[a]P levels of 49 ± 5.8 ug/kg, while mussels taken from the same body of water but remote from the pilings showed mean contamination levels of 2.1 ± 0.3 ug/kg. Samples of creosote-treated wood pilings (outer 4 mm) showed B[a]P levels averaging 570 ppm. Thin-layer chromatograms of piling extracts and of mussels growing on these pilings showed "similar fluorescent band patterns" and may indicate that the creosote migrated from the pilings into the mussels.

Dunn and Stich (1976) also measured the B[a]P content of mussels attached to and near a partially creosoted wharf. Creosoted pilings served as a bumper system around a concrete wharf, and a barricade of creosoted timbers was placed at one end of the wharf. Mussels taken from rocks underneath and near the wharf were contaminated with creosote, ranging from 54 to 78 ug/kg wet tissue weight; while those growing directly on the creosoted barricade were contaminated with 215 ug/kg, and those on rocks 1 meter from the barricade with 172 ug/kg. The authors suggested that the levels of B[a]P in mussels in this area are much higher than those generally found near creosoted structures and may reflect the age of the treated timber. The creosoted material at the wharf was relatively new and retained a tarry residue on its surface; mussels near older, weathered pilings should have much lower levels of B[a]P.

3. Effect on Freshwater Organisms

White (1975), in a study at a fresh water lake, compared an untreated pile, two pentachlorophenol-treated piles, an ammoniacal copper arsenate-treated pile, and a creosote-treated pile. After one month, the greatest number of algae species was growing on the surface of the creosote-treated pile. After one year all piles, except the one treated with ammoniacal copper arsenate, had extensive algal encrustment, along with many amphipods, limpets, and watermites entangled in the algal mats. Thus, creosoted piles did not affect the growth of attached freshwater organisms.

E. Regulatory History

Since 1966, various uses were cancelled and eliminated from the labels on coal tar and coal tar products. A summary of the cancelled uses follows:

February 1, 1966 - The U.S. Department of Agriculture (USDA) canceled the registrations of all products containing creosote used for disinfecting potato bins and other equipment used in potato production.

February 1, 1969 - USDA canceled the registrations of creosote and coal tar neutral oil-coal tar acid combination products used on beef cattle, goats, poultry, sheep, and swine.

February 26, 1970 - USDA canceled the registrations of products containing coal tar neutral oil-coal tar acid combinations used on dairy barns and the registration of products containing creosote used on animal sleeping quarters, barns, hog pens, and sheep folds.

March 12, 1971 - EPA canceled the registrations of coal tar neutral oil-coal tar acid combination products used on poultry houses.

II. Summary of Scientific Evidence Relating to Rebuttable Presumption

A. Oncogenicity

40 CFR Section 162.11(a)(3)(ii)(A) provides that "a rebuttable presumption shall arise if a pesticide's ingredient(s), metabolite(s), or degradation product(s)... induces oncogenic effects in experimental mammalian species or in man as a result of oral, inhalation, or dermal exposure..."

This discussion concerns only reports of the oncogenicity of coal tar, creosote, and coal tar neutral oil. Reports on the oncogenicity of soot, pitch, and petroleum, which have many constituents in common with coal tar, creosote, and coal tar neutral oil will not be discussed here.

In determining that the oncogenicity criterion was exceeded, the Working Group considered case reports of workers who were occupationally exposed to coal tar or creosote and who developed tumors, and reports of animal experiments in which mice, rats, or rabbits developed tumors from either dermal or inhalation exposure to coal tar, creosote, or coal tar products. In addition, the Working Group considered conclusions by the Carcinogen Assessment Group (CAG) (CAG, 1977; CAG, 1978; McGaughy, 1978) that coal tar, creosote, and coal tar neutral oil are oncogenic.

Also, the Working Group is aware that a number of polycylic and heterocyclic aromatic hydrocarbons present in coal tar creosote and coal tar have been well established as carcinogens [International Agency for Research on Cancer (IARC), 1973; Freudenthal and Jones, 1976; Committee on Biologic Effects of Atmospheric Pollutants, 1972]. Specifically, IARC (1973) reported that the following constituents of coal tar or creosote were carcinogenic to animals by one or more routes of administration: benz[a]anthracene, benzo[b]fluoranthene, benzo[j]fluoranthene, benzo[a]-pyrene, benzo[e]pyrene, chrysense, dibenzo[a,h]anthrancene, dibenzo[a,h]-pyrene, dibenzo[a,i]pyrene, indeno[1,2,3-cd]pyrene, benz[c]acridine, dibenz[a,h]acridine, and dibenz[a,j]acridine.

There may be differences in the chemical composition of the coal tars and coal tar derivatives in pesticide products subject to this presumption and the coal tar substances discussed in this section. If a registrant seeks to rebut the presumption on the ground that identified oncogens are not constituents of a particular pesticide product, the registrant should include relevant data on pesticide composition in the rebuttal submission.

1. Summary Table of Coal Tar, Creosote, and Coal Tar Neutral Oil Studies

Because of the numerous studies and reports on the oncogenicity of coal tar, creosote, and coal tar neutral oil, a summary table has been prepared and precedes the discussions of the studies (Table 2).

TABLE 2

SUMMARY OF COAL TAR, CREOSOTE, AND COAL TAR NEUTRAL OIL STUDIES

COAL TAR

Human Case Reports

Authors	Year	Substance and Type of Exposure	Occupation of Exposed Individual	Type of Tumor Response
Shambaugh	1935	Coal Tar on repair needle held between lips	Fishermen - Net loft workers	Epidermal carcinomas of the lower lip
Mauro	1951	Handling of Coal Tar Pitch	Tar distillery workers	Cancer of skin, scrotum, cheek, and lip
Rosmanith	1953	Hot Coal Tar Vapors	Tar barrel filler	Spinocellular cancer in scar of cured erythematous lupus infection.

COAL TAR

Animal Studies
Dermal Exposure

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Yamagiwa & Ichikawa	1915	Coal tar	Rabbits (Strain undefined)	Papillomas of the ear (site of application)
Tsuitsui	1918	Bituminous coal tar	Mice - English	Papillomas, carcinomas and spindle cell sarcoma
Kennaway	1925	Coal tar products of 450°C, 560°C, & 1,250°C distillation temperature.	Mice (Strain Undefined)	Skin tumors (higher rate of carcinogenesis at higher temperatures)

TABLE 2
(continued)

COAL TAR

Animal Studies
Dermal Exposure
(continued)

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Watson & Mellanby	1930	Dermal application of coal tar following dermal application of fats, oils, or tannic acid	Mice (Strain Undefined)	Increased tumor production
		Coal tar dermal application combined with addition of butter to diet	Mice (Strain Undefined)	Higher incidence of lung nodules
Bonser & Manch	1932	Scottish blast furnace tar; English crude tar	Mice (Strain Undefined)	Papillomas and squamous cell carcinomas of the skin
Gorski	1959	Coal tar	Mice (Bn Strain)	Skin tumors (some malignant)
Hueper & Payne	1960	Coal tar	Mice - Black (C57 Strain)	Skin carcinomas
Horton	1961	Coal tars, coal tar mixture, benzo[a]pyrene mixture	Mice (C3M Strain)	Skin tumors in 75% of each group of animals
		Coal tar distillates	Mice (C3M Strain)	Skin tumors
Deelman	1962	Coal Tar	Mice (Strain Undefined)	Skin carcinomas and papillomas
Shabad et al.	1971	Coal tar ointments	Mice (C57 CBA Hybrid Strain)	Skin tumors

TABLE 2
(continued)

COAL TAR

Animal Studies
Inhalation Exposure

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Horton	1961	Coal tar fumes preceeded by inhalation of formaldehyde; coal tar fumes	Mice (C3M Strain)	Both groups developed proliferative alveolar neoplasia; one mouse (group unspecified) developed a squamous cell carcinoma
Horton et al.	1963	Coal tar aerosol; Coal tar aerosol & gaseous formaldehyde	Mice (C3H Strain)	Both groups developed squamous cell tumors of lung and lung adenomas
Tye & Stemmer	1967	Coal tar; coal tar & phenolic & non-phenolic fractions of coal tar; non-phenolic fractions of coal tar	Mice (C3H/HeJ Strain)	Adenomas & carcinomas of the lung
Kinkead; McConnell & Specht; MacEwen & Vernot	1972-1974	Aerosolized coal tar - light oil & solid fraction removed	Mice (ICR-CF1) Mice (JAX-CAF1) Weanling rats (Sprague-Dawley) Yearling rats (Sprague-Dawley) Hamsters (Syrian golden) Rabbits (New Zealand white)	Mice developed skin tumors due to aerosolized material deposited on skin; Tumor response was not reported for rabbits, hamsters, or rats
MacEwen & Vernot; MacEwen et al.	1976	Aerosolized Coal tar	Mice (ICR-CF1) Mice (JAX-CAF1) Rats (Sprague-Dawley) Rabbits (New Zealand albino) Monkeys (Macaca Mullata)	Mice - Alveolargenic carcinoma and skin tumors; Rats - Squamous cell carcinomas; No tumor response was reported for rabbits or monkeys.

TABLE 2
(continued)

CREOSOTE

Human Case Reports

Authors	Year	Substance and Type of Exposure	Occupation of Exposed Individual(s)	Type of Tumor Response
Mackenzie	1898	Handling of Creosote	Worker who dipped railway ties in creosote	Warty elevation on arms; Papillomatous swellings on scrotum
O'Donovan	1920	Handling of Creosote	Workers who creosoted timbers	Skin cancer
Cookson	1924	Handling of Creosote	Creosote factory worker	Squamous epithelioma on hand; epitheliomatous deposits in liver, lungs, kidneys and heart walls
Henry	1947	Handling of Creosote	37 men of various occupations	Cutaneous epithelioma
Lenson	1956	Painting of Creosote	Shipyard worker	Malignant cutaneous tumors of the face

CREOSOTE

Animal Studies
Dermal Exposure

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Sall & Shear	1940	Creosote & benzo[a]pyrene	Mice (Strain A)	Accelerated tumor formation
Woodhouse	1950	Creosote oil	Mice (Albino; Undefined Strain)	Papillomas & carcinomas
Lijinsky et al.	1957	#1 creosote oil	Mice - Swiss	Papillomas & carcinomas

TABLE 2
(continued)

CREOSOTE

Animal Studies
Dermal Exposure
(continued)

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Poel & Kammer	1957	Blended creosote oils;	Mice (C57L Strain)	Papillomas & carcinomas metastatic growths in lungs & lymph nodes
		Light creosote oil	Mice (C57L Strain)	Papillomas
Boutwell & Bosch	1958	Creosote (Carbasota)	Mice (Albino - random bred)	Papillomas & carcinomas
Roe et al.	1958	Creosote oil (Carbasota)	Mice (Strain Undefined)	Skin & lung tumors

COAL TAR NEUTRAL OIL

Animal Studies
Dermal Exposure

Authors	Year	Substance Tested	Animal & Strain	Type of Tumor Response
Cabot et al.	1940	Benzene solution of neutral oil & benzo[a]pyrene	Mice - albino "market" mice	Inhibitory effect of tumor response as compared to tumor response with benzo[a]pyrene (effect credited to skin damage)
Berenblum & Schoental	1947	5 Coal tar neutral oil fractions	Mice (Strain Undefined)	All fractions but two were oncogenic
			Rabbits (Strain Undefined)	All fractions but one were oncogenic
Horton	1961	Coal tar neutral oils (maleic anhydride extracts)	Mice (Strain Undefined)	Produced tumors in 34.1 and 32.1 weeks

2. Coal Tar

a. Case Reports of Skin Cancer of Workers

Numerous reports of workers who developed cancer subsequent to coal tar exposure have been reported in the literature. The following is a summary of three of these case studies.

(1) Shambaugh

Shambaugh (1935) described his investigations of the incidence of cancer among fishermen and net loft workers who used and repaired tarred nets. Coal tar was used on nets to prevent them from rotting, and tar was often inadvertently smeared on the arms and face through use of the nets. Shambaugh's interest was prompted by the case of a patient who had sought medical help because of a growth on his neck. The growth was subsequently found to be an epidermal carcinoma involving the lymph nodes and invading the submaxillary gland. Closer examination of the patient additionally revealed a small, puckered scar on the lip, which the patient described as a "fisherman's sore." The patient had been a fisherman for 6 years, and while mending his nets he had held the tar-smeared needle between his lips at the spot where the growth developed. He had smoked a pipe but normally held it on the opposite side of his mouth. This case led Shambaugh to interview fishermen in Boston, Gloucester, New Bedford, and Provincetown, Mass. Using records of cases of cancer of the lip treated at Collis P. Huntington Memorial Hospital in Boston in 1932 and 1933, four fishermen with lip cancer were identified. Each had used tarred nets and at least one held the repair needle in the mouth on the side where the cancer developed. Tobacco was not used by this fisherman, but the other three smoked pipes. Two of the three cancers developed on the opposite side of the mouth from where the pipe was held.

Among net loft workers, three cancer cases were reported. All held the repair needle in the mouth, and at least one of these workers did not use tobacco. Two had died of lip cancer, while one was treated successfully with radium.

The exposure to tar through net repair needles in the eight cases ranged from 5-60 years. All were epidermoid carcinomas of the lower lip.

(2) Mauro

Workers in a tar distillery were examined by Mauro (1951). Of a crew of 32, 20 had significant exposure to tar (14 day laborers, 4 distillers, and 2 stokers). All except the two stokers had some type of skin disorder; four of these were cancers. A 61-year-old distiller developed cancer of the scrotum after a 30-year exposure. Treatment with surgery and radiation was unsuccessful, and the patient died. A 50-year-old distiller, employed for 25 years, developed cancer of the scrotum and forearm. He was also treated with surgery and radiation, but the outcome was not stated. A 64-year-old day laborer developed cancer of the cheek after a 30-year exposure and was cured with radiation. A 53-year-old day laborer developed lip cancer after 22 years of exposure. He was treated successfully with radiation. The author stated that the workers were exposed to both tar and pitch, and that the two substances produce essentially identical cancers.

(3) Rosmanith

Rosmanith (1953) described the case of a worker who developed skin cancer in the scar of a cured erythematous lupus infection. The patient had been employed for 10 years filling barrels with tar; while bending over the opening of the barrel, hot tar vapors had come in contact with his face. No protective gear was used other than gloves. The condition began at the root of the nose as several small solid growths which grew and expanded. The tumor was identified as a spinocellular cancer. Radiation treatment was unsuccessful.

b. Animal Studies - Dermal and Inhalation Exposure

The following 15 animal studies are presented chronologically. In general, they show that tumors were produced following dermal and inhalation exposure to coal tar. The Working Group notes that interpretation of some of the early studies is limited by the absence of control data. However, later studies which include appropriate control groups generally confirm and reinforce the observations in the early studies.

(1) Yamagiwa and Ichikawa

Yamagiwa and Ichikawa (1915) painted tar on the inner and outer surface and in open wounds of rabbits' ears. Seventy-one to 100 days following painting, papillomas were observed in 71% (12 of 17) of pairs of ears that had been painted on the inner surface. Papillomas were seen after 64 days in 17% (1 of 6) of rabbits' ears painted on the outer surface. Eighty-eight percent (7 of 8) of the ears painted on the inner surface had papillomas in rabbits surviving longer than 60 days. Only one papilloma was found in rabbits where the painting had been done on the outer surface or in a cut wound. The authors observed one eroded papilloma (site unspecified) that had the appearance of a carcinoma, but were unable to examine the tumor histologically. The authors felt that the inner surface of the ear was more susceptible to the development of papillomas than the outer surface of the ear because there were fewer hair follicles. The author did not report using any controls.

(2) Tsutsui Study

Tsutsui (1918) studied the tumor response from bituminous coal tar applied to the skin of "strong" English mice. The tar was applied every third or fourth day. A total of 259 mice in seven groups were used; however, only 67 mice survived for 100 days. Tumors were examined histologically and photographed.

Papillomas developed in 48% (32/67) of the mice that survived 100 days. Later some of the papillomas developed into carcinomas, which invaded adjacent tissue, and were found in 24% (16/67) of the mice. A spindle cell sarcoma was found in one mouse, and lung metastases, confirmed on histological examination, were present in two mice. The author did not report using any controls.

(3) Kennaway

A study of coal tar products of 450° C, 560° C, and 1,250° C distillation temperatures showed a higher rate of carcinogenesis at the higher temperature fractions (Kennaway, 1925). The tars were applied to the interscapular region of 100 mice twice a week. After 230 days, 50% (10/20) had skin tumors in the 1,250° C-tar group, 34% (10/29) had skin tumors in the 560° C-tar group, and 4% (2/49) had skin tumors in the 450° C-tar group. Most tumors were malignant in the 1,250° C and 560° C groups. Nearly half the animals in the 560°C and 1,250°C groups had died by day 173, and more died as the experiment continued. The author did not report using any controls.

(4) Watson and Mellanby

A study reported by Watson and Mellanby (1930) tested the carcinogenic effect on mice (undefined strain) of the combination of fats in the diet with dermal application of coal tar, of the combination of the dermal application of various fats, oils, or tannic acid prior to the dermal applicaton of coal tar, and of the combination of pretreatment of skin with petroleum ether to remove some of the fatty substances with skin application of coal tar. Four groups of 70 mice were dermally pretreated twice each week with fats (extracted from either normal mouse tissue or from mouse tissue of mice who had died from tar-induced tumors), olive oil, or tannic acid (first applied in the experiment as a 10% solution and later in the experiment as a saturated solution). Coal tar was applied to the skin 30 minutes later. Control groups of the same size were treated only with coal tar. There were no controls in which healthy animals were used for comparison. The animals were treated for 120 days and were observed for a subsequent 240-day period except in the case of the olive oil group which was observed for 20 days subsequent to 90 days of application. Fats were added to the diet by the addition of butter to the food. The mice were fed a diet of one part powdered bread and one part Sussex ground oats made into a moist paste with water. This diet was fed daily and was supplemented once weekly with cod liver oil and marmite. Butter was added in amounts varying from 12.5-25% of the diet of the test mice. A control group consisted of mice to which no butter was added to the diet but to which coal tar was dermally applied. There were no controls in which healthy animals were used for comparison. This experiment was done twice; once with 70 mice in both the test group and the controls and once with 90 mice in the test group and the controls.

Sixty male mice were treated with petroleum ether to remove at least some of the fatty substances in the skin. The petroleum ether (B.P. 60–80°C) was applied by means of a cotton-wool plug 30 minutes prior to the dermal tar application. This treatment was performed twice weekly for 120 days, and the mice were observed for an additional 330 days. A control group consisted of 60 male mice which were treated dermally with coal tar twice weekly for 120 days and then observed for 330 days. There were no controls in which healthy animals were used for comparison. An analysis of results of all the experiments is found in Table 3.

The application of tannic acid solution to the skin of mice prior to coal tar application did not affect incidence relative to the incidence produced by coal tar alone. The fat extracts or the olive oil, however, increased tumor incidence above the incidence produced by coal tar alone. Fat extracts from normal mice and from mice which had died from tar tumors increased tumor incidence to almost the same extent. Olive oil applied to the skin of mice prior to coal tar application resulted in a 72% lung tumor incidence among the skin tumor-bearing mice compared to 57% for controls (those treated with coal tar alone). The mice treated with fats or oils prior to tar treatment often developed tumors at several locations, which was not true of those treated with

TABLE 3

EFFECTS OF VARIOUS FATS AND OILS APPLIED DERMALLY OR IN THE DIET ON TUMOR INDUCTION BY COAL TAR (Watson and Mellanby, 1930)

Preconditioning	No. Tumors/ No. Animals	Percent of Tumor-Bearing Animals Developing Lung Tumors
I. Skin Treatments		
Experiment 1		
Tannic Acid	19/70 (27%)	47
Mouse Extract (Tumor-Bearing)	35/70 (50%)	63
Mouse Extract (Normal)	41/70 (59%)	59
Tar Only	18/70 (26%)	50
Experiment 2		
Olive Oil	29/70 (41%)	72
Tar Only	21/70 (30%)	57
II. Dietary Treatments		
Experiment 1		
Butter-fed	39/70 (56%)	60
No Butter	20/70 (29%)	37
Experiment 2		
Butter-fed	31/90 (34%)	55
No Butter	37/90 (41%)	41
III. Washing with Petroleum Ether		
Petroleum Ether (Wash)	19/60 (32%)	47
Tar Only	37/60 (62%)	61

tar alone. The addition of butter to the diet of two groups of mice led to a higher incidence of lung nodules in mice with tumors (60% vs. 37% and 55% vs. 41% in the two experiments), as compared to mice treated with tar with no dietary change. Butter-fed mice developed a greasy appearing coat. Mice washed with petroleum ether to remove some natural skin fats developed fewer skin tumors (32% vs. 62%), and fewer of those with skin tumors developed lung nodules than those mice treated with coal tar alone. The author concluded that addition of fats or oils to the skin or to the diet of mice prior to coal tar application caused more tar to be absorbed and thus increased tumor production. This conclusion was also supported by the reduction in tumor formation found when natural skin oil was partially removed by washing with petroleum ether.

(5) Bonser and Manch

Bonser and Manch (1932) studied the tumor response from application to mouse skin of three samples of Scottish blast-furnace tar, one sample of English crude tar, and an ether extract of the latter. The three samples of Scottish tar (I, II, and III) were made from coke-oven charges which contained in addition to the coal, 15-17%, 25%, and 10% coke, respectively; the English crude tar was made from a charge containing 75% coal and 25% coke. Sixty mice were used for testing each sample of tar. There was no control group. The hair was clipped away from a small area of skin in the region between the shoulder-blades. The tar was applied bi-weekly for the first 14 weeks, and thereafter once weekly because of marked ulceration of the skin of many mice. The study was continued for 56 weeks, by which time all the mice had died. Fifty-seven tumors were grossly identified. Thirty-one of the total 57 tumors which had developed were confirmed histologically. Results appear in Table 4.

In mice treated with the three Scottish samples, the first tumors appeared at the 16th week. The Scottish I, II, and III tar samples produced a tumor incidence of 7/60 (12%), 10/60 (17%), and 8/60 (13%) respectively. The tumors were malignant in three mice. The first tumor appeared at the 21st week when an English crude tar was used. Eight mice (13%) treated with the English crude tar and 24 mice (40%) treated with an ether extract of the English crude tar developed tumors. Nine tumors in mice given the ether extract were malignant. At 30 weeks there were 25 survivors in the latter group of mice, and over 50% had tumors.

The tumors were papillomas or squamous cell carcinomas of the skin. The carcinomas invaded the muscle. One malignant tumor, seen after 47 weeks of application of ether extract of English tar, consisted of a mass of "mononuclear round cells" invading the adjacent muscle and fat and metastasizing to the lymph nodes.

In this study, blast-furnace tar obtained from a variety of sources induced benign and malignant tumors of the skin in mice. The carcinogenic properties were enhanced by extraction with ether.

(6) Gorski

Gorski (1959) investigated the carcinogenic properties of two coal tars (one produced from coal from the "Bobrek" mine and one produced from coal from the "Nowa Huta" mine), a soft pitch, a hard pitch, and an anthracene fraction. Thirty Bn mice about 2.4 months old and of approximately equal sex distribution were in each test group. The authors did

See 19A.

TABLE 4

INCIDENCE OF SKIN TUMORS IN MICE TREATED WITH BLAST FURNACE TARS
Carcinogen Assessment Group (CAG), 1978

Tar Sample	Number of Tumors per Number of Animals	Appearance of First Tumor (weeks)	Malignant Tumors
Scottish I	7/60 (12%)	16	0/60 (0%)
Scottish II	10/60 (17%)	16	2/60 (3%)
Scottish III	8/60 (13%)	16	1/60 (2%)
English Crude	8/60 (13%)	21	0/60 (0%)
Ether Extract of English Crude	24/60 (40%)	12	9/60 (15%)

not report using a control group. The mice were described as having a "low threshold for spontaneous growths." One drop of the test solution was applied to the skin near the backbone of the mice twice a week for 5 months, for a total of 44 applications per mouse. No data were provided on controls.

The test solutions were prepared by dissolving the materials in benzene (a 1:1 ratio). Pitch, being insoluble in benzene, was extracted using Soxhlet's apparatus, which provided a 1:5 solution in benzene.

Skin changes observed included peeling, swelling, and wart-like growths of differing shapes and sizes. Skin effects appeared earliest and with greatest intensity in the soft pitch group. Tumor results are reported in Table 5.

After 8 weeks, some mice had died in each group. Skin tumor observations were made at 4 months. Tar from the "Bobrek" mice produced an average of 0.6 tumors per mouse in 22 mice; 6 had malignant tumors. Eight of 26 surviving mice in the Nowa Huta mine tar group had malignancies, and there were, on the average, 0.2 tumors per animal. Twenty-one mice survived in the hard pitch group, with an average of one tumor per mouse; eight had malignant tumors. In the soft pitch group, 28 mice survived, with an average of 2.9 tumors each; 14 mice had malignant tumors. Of those to which an anthracene fraction was applied, 24 mice survived with an average of 0.3 tumors each; 4 mice had malignancies.

Mice with skin changes in all groups were debilitated and died by the end of the seven-month experiment. White hard growths ranging in size from that of a pinhead to that of a peppercorn were found by

TABLE 5

TUMOR PRODUCTION IN MICE DERMALLY EXPOSED TO NOWA HUTA COAL TAR, POBREK COAL TAR, HARD PITCH, SOFT PITCH OR AN ANTHRACENE FRACTION
(Adapted from Gorski, 1959)

Product Tested	No. of Mice At Onset of Experiment	After Eight Weeks	Average No. of Tumors/mouse (after 4 months)	No. of Malignant Tumors Proven Histologically 1/
Pobrek Tar	30	22	0.6	6/22 (27%)
Nowa Huta Tar	30	26	0.2	8/26 (31%)
Hard Pitch	30	21	1.0	8/21 (38%)
Soft Pitch	30	28	2.9	14/28 (50%)
Anthracene Fraction	30	24	0.3	4/24 (17%)

1/ The denominator is the number of mice in that group alive after eight weeks.

dissection of the skin tumors, particularly in the later stages of the experiments. Other changes included enlarged lymph nodes, growths in the lungs, flaccidity of the liver, pale hard growths on the kidneys, and degeneration of the liver and kidneys. Metastases to the lymph nodes were confirmed in mice from the soft and hard pitch groups.

The author concluded that all the products tested were carcinogenic, that soft pitch was the most carcinogenic, anthracene fraction the least carcinogenic, and the two tars and the hard pitch were in an "intermediate" group.

(7) Hueper and Payne

Hueper and Payne (1960) found that skin tumors were produced in mice following the application of coal tar. Coal tar, four petroleum road asphalts (Venezuelan, Mississippian, Oklahoman, and Californian), one petroleum roofing tar, and paraffin oil were applied to the napes of the necks of groups of 50 black C57 mice (25 of each sex) for two years. An untreated control group consisted of 200 mice. So that the materials could be applied as droplets, the coal tar and roofing asphalt were heated to make them liquid, and the road asphalts were diluted with a sufficient amount of acetone. The paraffin oil was painted on the skin. Postmortem examinations were performed on all mice, and histological examinations were made of all tissues which exhibited gross abnormalities. The results are found in Table 6.

Carcinomas of the skin were found in 22 of 50 (44%) and papillomas in one of 50 (2%) mice receiving dermal applications of coal tar, whereas control mice did not develop tumors of the skin.

TABLE 6

SKIN TUMORS IN MICE GIVEN DERMAL APPLICATIONS OF COAL TAR, PETROLEUM ROOFING TAR, PARRAFIN OIL, OR PETROLEUM ROAD ASPHALTS
Carcinogen Assessment Group (CAG), 1978

Treatment	Skin Carcinomas	Skin Papillomas	Total
Control	0/200 (0%)	0/200 (0%)	0/200 (0%)
Coal Tar	22/50 (44%)	1/50 (2%)	23/50 (46%)
Petroleum Roofing Tar	1/50 (2%)	0/50 (0%)	1/50 (2%)
Paraffin Oil	1/50 (2%)	1/50 (2%)	2/50 (4%)
Petroleum Road Asphalt			
Venezuelan	0/50 (0%)	0/50 (0%)	0/50 (0%)
Mississippian	1/50 (2%)	1/50 (2%)	2/50 (4%)
Oklahoman	0/50 (0%)	1/50 (2%)	1/50 (2%)
Californian	1/50 (2%)	0/50 (0%)	1/50 (2%)

Hueper and Payne also administered some of the substances via inhalation and intramuscular injection. Coal tar did not produce lung tumors in rats or guinea pigs inhaling such fumes for periods up to two years but did produce muscle sarcomas following intramuscular injection. The results of the intramuscular study are not discussed here because intramuscular injection is not a route of exposure included in the criteria of 40 CFR 162.11(a)(3)(ii)(A).

(8) Horton

In several experiments Horton (1961) tested a number of crude coal tars, coal tar distillates, and fractions of coal tar for skin tumor response in C3M mice. In the first part of the study, five coal tars (four from the coking of bituminous coal and one from the coking of lignite coal), a mixture of one of the bituminous coal tars in 50% benzene, and a benzo[a]pyrene mixture were tested. The authors did not report using a control group. No data were provided on the number of mice tested nor on the length of time the animals were treated; however, the time-to-tumor for each group was reported. The incidence of tumors was reported to be greater than 75% (only a percentage was reported) for each test group. Horton developed a numerical index designed to grade the various tars and tar fractions for relative carcinogenic potency. This index was referred to as the potency for a minimum concentration of material (PMC). A high PMC value is meant to indicate a greater carcinogenic potency. For tars D-1 and D-613 for which multiple doses were applied, a dose response was evident. The mean time-to-tumor (in weeks), the schedule of application, and the PMC values for each of the tars, the tar solu-

TABLE 7

MEAN TIME-TO-TUMOR AND PMC VALUES FOR FOUR BITUMINOUS TARS, ONE LIGNITE TAR, AND ONE SOLUTION OF BENZO[a]PYRENE (Adapted from Horton, 1961)

Treatment	Schedule of Application (#/week - mg)	Mean Time-to-Tumor (weeks)	PMC
D-1 - bituminous tar	2-10	15.6*	0.27*
	2-50	12.6*	0.37*
	3-100	7.0*	0.63*
D-4 - bituminous tar	2-10	24.8	0.13
D-5 - bituminous tar	2-10	23.6	0.14
D-5A - 50% dilution by weight of D-5 tar	2-10	25.1	0.13
D-8 - bituminous tar	3-50	21.9	0.11
D-12 - lignite tar	3-50	17.1	0.16
D-613 - benzo[a]pyrene in 85% beta-methylnapthalene and 15% benzene solution	2-15	33.0*	0.08*
	2-50	30.6*	0.10*

---

* The multiple doses for Tars D-1 and D-613 demonstrated a mean time-to-tumor and a PMC dose responses.

tion, and the benzo[a]pyrene solution are reported in Table 7.

Two tars from the previous group (D-1 and D-8) were chosen to test the effect of skin washing with a detergent in water 5 or 60 minutes after tar application. Tars D-1 and D-8 had the highest (0.8) and lowest (0.1) benzene-insoluble content, respectively. Washing delayed tumor development, but the final tumor incidence was not significantly changed. The delay was greater in the animals washed 5 minutes after dermal application.

Horton also determined the relationship between the amount of benzo [a]pyrene in distillates of coal tar and the carcinogenic potency of those distillates. Tar D-1, a distillate oil of D-1 (the first 9-13.5% of the distillation), a proportionate reblend of nine distillate fractions of D-1, and two distillate fractions (a carbolic oil and a light creosote oil) of a coal tar (D-9) not previously used in the experiments were tested for B[a]P content and carcinogenic potency (PMC) to the skin of mice. With the exception of Tar D-1, all test materials were applied to mice (strain unspecified) in 10 mg doses. Tar D-1 was applied in 20 mg doses. The number of applications was described as "repeated," but neither the frequency nor the duration was specified. The PMC values and benzo[a]pyrene content of the test substances are reported in Table 8.

Comparison of the benzo[a]pyrene content with the carcinogenic potencies of various fractions showed that no tumors were produced by those fractions in which no benzo[a]pyrene could be detected, while the carcinogenic potency of the test materials that contained benzo[a]pyrene was correlated with their content by weight of this carcinogen. Despite this observation, the authors did caution that these results do not imply that benzo[a]pyrene is the only carcinogen in these substances.

TABLE 8

PMC VALUES AND BENZO[a]PYRENE CONTENT FOR TWO COAL TARS, SEVERAL DISTILLATES OF THOSE COAL TARS, AND A PROPORTIONATE REBLEND OF THE DISTILLATES FROM ONE OF THE TARS

Test Material	Doses (mg)	Content of Benzo[a]pyrene (%)	Relative Carcinogenic Potency (PMC)
Tar D-1	20	0.74	0.27
Distillate Oil of Tar D-1	10	0.01	0.01
Proportionate Reblend of the Nine Cuts of Tar D-1	10	0.08	0.11
Carbolic Oil of Tar D-9	10	0.00	0.00
Light Creosote Oil of Tar D-9	10	0.00	0.00

(9) Deelman

Deelman (1962) studied the effect of time between tar applications on tumor development. He found that papillomas developed after 18 applications regardless of the interval between applications (2 to 7 days). The number of carcinomas was small after 18 applications. In time, after the end of the applications, however, many of the papillomas became carcinomas.

When tar was applied to different size skin areas or fields, it was found that mice with the largest field (20 x 25 mm) had an average of one carcinoma and seven papillomas each. Eight mice, with a tarred field of 2.5 x 25 mm (The coal-tarred area for the eight mice combined is equal to the largest field tested or 20 x 25 mm field for one mouse.) had a total of 34 papillomas and three carcinomas among them. It was found that among the tar fields tested (20 x 25 mm, 10 x 25 mm and 2.5 x 25 mm), the smaller the tar field, the larger the number of tumors per unit area. This may be a result of the greater toxicity to the animals with the larger tar fields; the author observed that mortality, weight loss, and kidney damage increased as the size of the tar field increased. No untreated controls were used in the study.

(10) Shabad et al.

Shabad et al. (1971) applied three coal tar ointments [Locacorten tar ointment (USA), CIBA coal tar ointment (Switzerland), and coal tar ointment (USSR)] to C57 CBA hybrid mice two or three times each week for 10 or 12 months to test for tumor production. The authors did not report using any control groups. All of the mice died within 18 months or were sacrificed because of their poor condition. Eighteen of 19 (94.7%), 20 of 21 (95.2%), and 16 of 17 (94.1%) of the animals in USSR, CIBA, and Loracorten ointment groups, respectively, developed tumors. The benzo [a]pyrene content of the three ointments was 225, 5,020, and 5,190 ug/g, respectively. Shabad also tested the effect of two birchwood tar ointments, Vishnevsky and Tashkent, on groups of 20 and 24 C57CBA mice. None of the mice in the groups develped tumors after 18 months. The benzo[a] pyrene contents of the Vishnevsky and Tashkent tars were 0.0013 and 0.044 ug/g, respectively.

(11) Horton

Horton (1961) studied the lung tumor response in C3H mice after exposure to coal tar fumes. One group of mice inhaled formaldehyde-contaminated air intermittently for an unspecified amount of time, while a second group was kept in clean air. The former group developed squamous metaplasia as a result of their exposure to formaldehyde. Both groups were then exposed to coal tar fumes (0.33 mg/liter) for one hour/day, three days/week for 13 to 33 weeks. A majority of the mice (numbers were not reported) in both groups developed proliferative alveolar neoplasia, and one (the group was not reported) developed a squamous cell carcinoma. The two groups of mice showed no difference in neoplasia incidence. A third group of mice, exposed intermittently to formaldehyde alone for 64 weeks, showed no alveolar proliferation or carcinoma development.

(12) Horton et al.

Horton et al. (1963) examined C3H mice (a strain that was reported to have a low historical incidence of spontaneous pulmonary adenomas) for lung tumors following inhalation exposure to coal tar aerosol, gaseous formaldehyde, or gaseous formaldehyde followed by coal tar aerosol. In the first part of the experiment, groups of 60, 60, and 42 mice were exposed to concentrations of 0.5, 0.10, or 0.20 mg/liter, respectively, of gaseous formaldehyde for three 1-hour periods per week. The control group consisted of 59 untreated mice. After 35 weeks, none of the animals that were sectioned of those that died (118 of 221) during the 35-week period had developed lung tumors. The surviving animals were used to conduct further experiments with coal tar and formaldehyde. The surviving 33 mice from the control group in the first part of the experiment and the surviving 26 mice from the group in the first part of the experiment that had been exposed to 0.10 mg/l of gaseous formaldehyde were exposed to 0.30 mg/l of coal tar aerosol for three 2-hour periods per week for up to 36 weeks. The surviving 36 mice from the group that had been exposed to 0.05 mg/l of formaldehyde in the first part of the experiment were exposed to 0.15 mg/l of formaldehyde for three 1-hour periods each week for up to 35 weeks. There was also an untreated control group[1/] which was observed for 82 weeks.

The test animals were exposed to the test substances until death; the first death occurred 1 to 11 weeks after exposure and the longest time until death was 36 weeks. Serial sections of the trachea, large bronchi, and lung from the exposed animals and from the lungs of 30 unexposed mice were examined (Table 9).

[1/] The initial size of the untreated group was not reported. At the termination of the experiment at 82 weeks, the group consisted of 30 mice.

TABLE 9

TUMORS OF THE LUNG IN MICE INHALING FORMALDEHYDE AND/OR AEROSOL OF COAL TAR

Carcinogen Assessment Group (CAG), 1978

Treatment	Squamous Cell Tumors	Adenomas	Total
(-)	0/30 (0%)	0/30 (0%)	0/30 (0%)
Coal Tar	6/33 (18%)	1/33 (3%)	7/33 (21%)
Formaldehyde and Coal Tar	1/26 (4%)	1/26 (4%)	2/26 (8%)
Formaldehyde	0/36 (0%)	0/36 (0%)	0/36 (0%)

Five mice inhaling coal tar aerosol and one mouse inhaling formaldehyde followed by coal tar developed squamous cell tumors in the periphery of the lung, involving 1/3 to 1/2 of the lobe. In two mice from the former group, several lobes were involved. A sixth mouse in the former group that died after 20 weeks of exposure had an invasive squamous cell carcinoma, which was described as "unquestionably a squamous cell carcinoma whereas those occurring in the other five animals probably represented an earlier stage of development at the time of death." One mouse in each group had adenoma of the lung. Tumors of the lung were not observed in mice breathing formaldehyde only or in untreated controls.

There were other changes produced in the tracheobronchial epithelium as the result of the inhalation of coal tar. The most striking was a necrotizing tracheobronchitis in the majority of mice; the incidence was not reported. In addition, squamous cell metaplasia extended into the smaller bronchi. Hyperplasia of the bronchial epithelium occurred frequently, sometimes with papillary infolding. The epithelium of untreated mice was normal showing neither metaplasia nor hyperplasia.

Epithelial changes in mice inhaling formaldehyde involved mostly the trachea; extension into the major bronchi was infrequent and did not occur at all in the smaller bronchi. In general, the inhalation of formaldehyde resulted in an acute tracheobronchitis ranging from slightly to severely necrotizing, or developing into a chronic type with proliferation of fibrous tissue. This was sometimes complicated by bronchopneumonia. In summary, mice inhaling coal tar aerosol developed squamous cell carcinomas of the lung, as well as hyperplastic and metaplastic epithelial changes.

(13) Tye and Stemmer

Tye and Stemmer (1967) separated two different coal tars into phenolic (P-tar) and nonphenolic (N-tar) fractions and exposed mice by inhalation to various blends of the coal tar fractions and to one of the original tars. The same coal tar (T-1) (Specific gravity 1.17, 4.5% tar acid, 0.7% benzo[a]pyrene and 67% Diels-Adler compounds) that was used in the experiments by Horton, Tye, and Stemmer (1963) and a second, somewhat different tar (T-2) (Specific gravity 1.24, 1.4% tar acid, 1.1% benzo[a]pyrene, and 2% Diels-Alder compounds), were the two tars from which the phenolic (P-tar) and nonphenolic (N-tar) fractions were separated.

Fifty male C3H/HeJ mice, three to five months old, were in each test group. The tests groups consisted of untreated, Tar-1, N-Tar-1, N-Tar-1 plus P-Tar-1, N-Tar-1 plus P-Tar-2, and N-Tar-2 plus P-Tar-1. Mice were exposed for two hours every three weeks. During the first eight weeks, the exposure was at a concentration of 0.20 mg/l, but this was reduced to 0.12 mg/l because so many mice died.

Three mice from each group were killed after four weeks, and five mice were killed after 31 weeks. Surviving mice were killed at the end of 55 weeks. Mortality from exposure was high in all groups of treated mice. At the end of the experiment, there were 31/50 (62%), 11/50 (22%), 11/50 (22%), 10/50 (20%), 21/50 (42%), and 21/50 (42%) mice alive in the control, Tar-1, N-Tar-1, N-Tar-1 plus P-Tar-1, N-Tar-1 plus P-Tar-2, and N-Tar-2 plus P-Tar-1 groups, respectively. Tumor response is recorded in Table 10.

The most prominent lesions were intrabronchial adenomas and ade-

TABLE 10

INCIDENCE OF LUNG TUMORS IN MICE INHALING AEROSOLS OF COAL TARS[1/]
Carcinogen Assessment Group (CAG), 1978

Treatment	Metaplasia		Adenomas[2/]		Adenocarcinomas		Adenomas & Carcinomas	
(-)	0/32	(0%)	0/32	(0%)	0/32	(0%)	0/32	(0%)
Tar-1	5/13	(38%)	12/13	(92%)	3/13	(23%)	13/13	(100%)
N-Tar-1	2/20	(10%)	16/20	(80%)	0/20	(0%)	16/20	(80%)
N-Tar-1 + P-Tar-1	5/19	(26%)	14/19	(74%)	1/19	(5%)	15/19	(79%)
N-Tar-1 + P-Tar-2	7/25	(28%)	14/25	(56%)	1/25	(4%)	15/25	(60%)
N-Tar-2 + P-Tar-1	4/23	(17%)	14/23	(61%)	0/23	(0%)	14/23	(61%)

[1/] Mice surviving for 46 weeks or longer.

[2/] Includes intrabronchial and alveolar adenomas.

nocarcinomas, occurring anywhere in the bronchial tree. Multiple tumors were frequently seen. The intrabronchial adenomas were papillary. There also were alveloar adenomas which were peripheral. Tumors of the lung were diagnosed as adenocarcinomas only if there was invasion or if metastases were observed.

Adenomas and carcinomas of the lung were observed in 60% to 100% of the mice inhaling aerosols of coal tars, whereas tumors were not seen in any of the control mice. Incidences of squamous metaplasia varied from 10% to 38% in treated mice and were absent in control mice. "Alveolar epithelization" was also observed, but less often than squamous metaplasia. Areas of squamous and alveolar metaplasia were not considered as tumors, even when they occupied relatively large spaces.

(14) Kinkead, McConnell and Specht, and MacEwen and Vernot

MacEwen and Vernot (1972-1974), Kinkead (1973), and McConnell and Specht (1973) reported on a study in which mice, rats, hamsters, and rabbits were exposed to a coal tar aerosol from which the light oil and solid fraction was removed. Gross skin pathology for the mice was reported; any other tumor response in the mice and in the other animals was not reported.1/

Groups of 64 female yearling and 64 weanling (32 of each sex) Sprague-Dawley rats, 50 male JAX-CAF1 mice, and 50 male ICR-CF1 mice were

---

1/ Per contractual agreement, Sasmore performed internal and skin histopathology for the study and reported his results (Sasmore, 1976), but because information in the Sasmore report is incomplete, no conclusions can be made about the report.

exposed continuously for 90 days (except for 15 minutes a day to allow for animal maintenance) to concentrations of 0.2, 2.0, and 10.0 mg/m^3 of coal tar aerosol. Eighty-two female yearling Sprague-Dawley rats, 82 weanling Sprague-Dawley rats (73 female and 9 male), 75 male JAX-CAF1 mice, 75 male ICR-CF1 mice, 100 male golden Syrian hamsters, and 24 New Zealand white rabbits were exposed continuously, as above, for the same 90-day period to a concentration of 20 mg/m^3. The control animals consisted of 41 female and 41 male Sprague-Dawley weanling rats, 61 female Sprague-Dawley yearling rats, 75 male JAX-CAF1 mice, 75 male ICR-CF1 mice, 24 female New Zealand white rabbits, and 100 male golden Syrian hamsters (MacEwen and Vernot, 1974). Many of the mice contracted a streptococcus infection and died before 93 days post exposure. Skin tumor response for the mice is found in Table 11.

Tumor responses of 28% (10 of 36), 30% (3 of 10), and 8% (2 of 25) were seen in the three highest dose groups of the ICR-CF1 mice; no tumors (0 of 62) were found in the controls. A tumor response of 37% (10 of 27) was found in the highest dose group in the JAX-CAF1 mice; no tumors (0 of 74) were found in the JAX-CAF1 controls. McConnell and Specht (1973) examined some of the skin tumors histologically and concluded that a whole spectrum of epithelial tumors, from squamous cell papilloma to keratoacanthoma, to "frankly aggressive" appearing squamous cell carcinoma are stimulated by the coal tar aerosol, although the majority of these tumors fall in the squamous cell carcinoma category. McConnell and Specht also found a time-to-tumor dose response for the coal tar aerosol. This dose response is shown in Table 12. As stated above, tumor response was not reported for the rats, hamsters, or rabbits.

TABLE 11

TUMOR RESPONSE IN MALE ICR-CF1 AND JAX-CAF1 MICE FOLLOWING EXPOSURE COAL TAR AEROSOL (Adapted from McConnell and Specht, 1973)

Dose (mg/m^3)	ICR-CF1[1]		JAX-CAF1[1]	
20.0	10/36	(28%)[2]	10/27	(37%)[2]
10.0	3/8	(38%)[3]	0/12	(0%)[3]
2.0	2/25	(8%)[3]	0/47	(0%)[3]
0.2	0/2	(0%)[3]	0/47	(0%)[3]
0.0	0/62	(0%)[2]	0/74	(0%)[2]

---

[1] The numerator is the number of animals with tumors at 415 days post exposure. The denominator is the number of animals that were alive at 93 days post exposure.

[2] This dose group began with 75 animals.

[3] This dose group began with 50 animals.

TABLE 12

LATENT PERIOD OF FIRST TUMOR INDUCTION IN CTV-I EXPOSED ICR-CF1 MICE (McConnell and Specht, 1973)

Dose (mg/m^3)	Time of Tumor Appearance (Days)
20	< 93
10	128
2	142

(15) MacEwen and Vernot, and MacEwen et al.

MacEwen and Vernot (1975 and 1976) and MacEwen et al. (1976) reported on the studies of the tumor response of mice, rats, rabbits, and monkeys following exposure to coal tar aerosol. In the first study, 60 female Sprague-Dawley yearling rats, 80 Sprague-Dawley weanling rats (40 males and 40 females), 75 JAX-CAF1 male mice, 75 ICR-CF1 male mice, and 100 male golden Syrian hamsters were exposed continuously for 90 days (except for 15 minutes a day to allow for animal maintenance) to concentrations of 0.2, 2.0, and 10.0 mg/m^3 of coal tar aerosol. An equal number of each species were used for controls. The coal tar used to generate the aerosol in this study was:

> a composited mixture collected from multiple coking ovens around the greater Pittsburgh area. The coking ovens were of several different types and used different coal sources for their starting materials. The coke oven effluents were collected in air collection devices using a chilled water spray to condense the higher boiling distillate fractions. After settling and separation of the liquid phase, the various coal tar samples were blended together with a 10% by volume amount of the BTX (benzene; toluene; xylene) fraction of the coke oven distillate.

An aerosol particle size determination in the exposure chambers was performed, and it was found that a minimum of 97% of all droplets were in a respirable range of five microns or less in diameter. Only skin tumor response for the mice was reported (Table 13). Tumor response was not reported for the hamsters or rats.

In the second study 75 female and 100 male ICR-CF1 mice (described as tumor susceptible), 50 female JAX-CAF1 mice (described as a tumor resistant hybrid strain), 40 male and 40 female CFE strain Sprague-Dawley wean-

TABLE 13

SKIN TUMOR RESPONSE IN ICR-CF1 AND JAX-CAF1 MICE FOLLOWING EXPOSURE TO COAL TAR AEROSOL (MacEwen and Vernot, 1976)

Dose (mg/m^3)	Week of Observation [2]	Cumulative Number of Tumors [1]			
		ICR-CF1		JAX-CAF1	
		Exposed	Control	Exposed	Control
10	100	44/75 (59%)	3/75 (4%)	18/75 (24%)	1/75 (1%)
2	103	14/75 (19%)	0/75 (0%)	3/75 (4%)	0/75 (0%)
0.2	101	1/75 (1%)	0/75 (0%)	1/75 (1%)	1/75 (1%)

1/ The numerator is the number of animals with tumors; the denominator is the number of animals exposed.

2/ Includes the 90-day exposure period.

ling rats, 18 New Zealand albino rabbits, and 5 male and 9 female Macaca mulatta monkeys were exposed to 10 mg/m^3 of coal tar aerosol for 6 hours each day, five days per week for 18 months. The coal tar used to generate the aerosols in this study was the same as that of the first study. Aerosol particle size was determined monthly in the exposure chambers. A minimum of 99% of the total droplets in both chambers were 5 microns or less in diameter and were thus within a respirable size range for rodents.

Exposure to the coal tar at 10 mg/m^3 significantly reduced the body weight of rabbits and rats compared with the controls, whereas monkeys showed no significant change in body weight. Sixteen of 18 rabbits and six control mice died during the test period. These deaths were attributed to a chronic respiratory infection which caused debilitation and dehydration. At the conclusion of the exposure period, the test monkeys and the surviving test rabbits along with the unexposed controls were delivered to the NIOSH Laboratories in Cincinnati, Ohio, for long-term post-exposure observation, but the results were not reported in MacEwen et al. (1976). Discussion with MacEwen indicated that while the monkeys are still under observation, the number of surviving rabbits (2 of 18) was too few for statistical comparison, and those animals were sacrificed (Gibb, 1978a). No tumor response was found in the sacrificed rabbits (Gibb, 1978b).

Alveolargenic carcinomas were produced in 26 of 61 (43%) ICR-CF1 mice and in 27 of 50 (54%) JAX-CAF1 mice. The number of tumors in the ICR-CF1 and the JAX-CAF1 control mice were 3 of 68 (4%) and 8 of 48 (17%), respectively. The exposed and control groups did not differ in the incidence of other types of tumors including squamous cell carcinomas, lymphosarcomas, subcutaneous sarcomas, alveolargenic adenomas, bronchiogenic carcinomas, reticulum cell sarcomas, hemangiosarcomas, and hemopoietic tumors.

Skin tumors were produced in 5 of 75 (7%) of the ICR-CF1 mice and 2 of 50 (4%) of the JAX-CAF1 mice as compared to 3 of 75 (3%) and 1 of 50 (2%) in the ICR-CF1 and JAX-CAF1 controls, respectively. The criterion for counting a lesion as a skin tumor was a growth greater than 1 mm in diameter and in height. Each tumor was ultimately confirmed by histologic examination. MacEwen et al. compared the lack of skin tumor response in the second study to the tumor response of the 10 mg/m^3 dose group of the first study. As stated previously, the first study found a skin tumor incidence of 44 of 75 (59%) in the treated ICR-CF1 mice and 18 of 75 (24%) in the treated JAX-CAF1 mice as opposed to only three of 75 (4%) in the ICR-CF1 controls and 1 of 75 (1.3%) in the JAX-CAF1 controls, respectively. A calculation of total exposure time (MacEwen et al.,1976) revealed that the same amount of coal tar aerosol reached the skin of the mice in the second study as in the first study. MacEwen et al. suggested that the 18 months' intermittent exposure of the animals in their study allowed the animals enough time each day to permit normal cleaning of the fur.

The incidence of coal tar tumorigenesis in rats is reported in Table 14.

The incidence of squamous cell carcinomas in the lungs was (38/38) 100% in exposed males and (31/38) 82% in exposed females as opposed to 0 of 36 (0%) in male controls and 0 of 37 (0%) in female controls.

A dose-related tumor response was observed for both the ICR-CF1 and the JAX-CF1 mice.

TABLE 14

COAL TAR TUMORIGENESIS IN RATS
(MacEwen, 1976)
et al.

	Controls		Exposed	
	Males	Females	Males	Females
Number Examined Histologically[1/]	30	37	38	38
Number of Rats with Tumors:				
Squamous Cell Carcinoma, Lung	0	0	38	31
Squaceous Cell Carcinoma	0	1	0	0
Intraabdominal Carcinoma	0	1	0	0
Mammary Fibroadenoma	0	1	0	3
Mammary Adenocarcinoma	0	1	0	0
Other Tumors	0	1	8	2
Overall Tumor Incidence (%)	0	13	100	82

[1/] The original number of rats per group was 40. However, because of autolysis and/or cannibalization, a few animals were unsuited for histopathological examinations.

Many aromatic hydrocarbons such as those found in coal tar are known to fluoresce. Mice (skin and hair) tissue samples taken during the exposure period from the ICR-CF1 mice in the second experiment were extracted with toluene and analyzed for fluorescent content. Results are found in Table 15. Mice fluorescence during exposure correlated with the tumor response.

3. Creosote

Reports of workers who developed cancer subsequent to creosote exposure have been reported in the literature. The following is a chronological summary of these reports.

a. Case Reports of Skin Cancer in Workers

(1) Mackenzie

Mackenzie (1898) reported the case of a man employed for 30 years dipping railway ties in liquid creosote in an air-tight chamber. The worker stated that only his arms and hands came into contact with the dripping planks. In several places on his forearms, there were "skin elevations of a warty character about the size of split peas." On the right half of the patient's scrotum were several papillomatous swellings from the size of a pea to that of a nut, rather soft but covered with a horny crust and sore to the touch. The patient had picked several off, leaving a bleeding surface. The author suggested that the tumors were likely to become epitheliomatous.

(2) O'Donovan

O'Donovan (1920) lists three cases of skin cancer of men occupationally exposed to creosote; two of the men creosoted wood, and one pickled wood in creosote. O'Donovan detailed the case of one man who

TABLE 15

SUMMARY OF HIDE FLUORESCENCE (ug/cm^2) OF ICR-CF1 MICE DURING AND AFTER EXPOSURE TO COAL TAR AEROSOL

Dose (mg/m^3)	Days of Exposure					30 Days Post-Exposure	ICR-CF1 Mouse Skin Tumors at 100 Weeks
	1	7	30	60	90		
10.0	26.9	34.9	19.2	23.8	21.6	0	44/75 (59%)
2.0	2.4	9.3	7.6	4.4	9.9	0	14/75 (19%)
0.2	0.4	1.6	4.9	1.0	3.8	0	1/75 (1%)

had been creosoting timber for 40 years. Warts had appeared on his hands, legs, and behind his ears seven years prior to reporting his case. The warts had fallen off and left scars behind them. Eighteen months before the case was reported, a wart on the patient's scrotum had fallen off, leaving a small sore which never healed and steadily enlarged. Three months before admission to the hospital, the glands of the left groin enlarged; the patient steadily lost weight and grew weaker. On admission to the hospital, the case was considered inoperable.

(3) Cookson

Cookson (1924) reported on a worker employed for 33 years to carry creosoted wood. At least 15 years before the case was reported, a small swelling appeared on the back of the worker's right hand. The swelling would occasionally break open and then heal again. About 7 years later, the swelling increased substantially in size until the growth had to be removed. A portion was examined histologically prior to being excised and proved to be a squamous epithelioma. Following the patient's death several years later, an autopsy was performed, and small secondary epitheliomatous deposits were found in the liver, both lungs, and in both kidneys. There were also two secondary deposits in the heart walls. One in the left ventricular wall involving its whole thickness was the size of a walnut and was beginning to break down in the interior. The other was the size of a pea at the right border of the right ventricle.

(4) Henry

Henry (1947) reviewed 753 cases of cutaneous epitheliomata reported to the British Medical Inspector of Factories from 1920 to 1945 and found 37 cases attributable to creosote exposure. Of these cases 14 occurred among workers treating timber, 9 among people handling creosote in storage, and 10 among people using creosote as a releasing agent for brick molds. One case of epithelioma was reported among workers using creosote for the manufacture of furnace crucibles, and one case among workers manufacturing creosote disinfectants. The author also reports two cases of cutaneous cancer not reported to the British Medical Inspector of Factories: a railway platelayer handling creosoted ties and an assistant chemist testing creosote for 16 months in a tar distillery laboratory.

(3) Lenson

Lenson (1956) described a shipyard worker who had worked with creosote for three years. Malignant cutaneous tumors of the face appeared 5 years after working with the creosote. The worker had been a painter for 41 years and had mixed his own paints, using lead and oils. Turpentine and white gasoline had been used as paint removers.

b. Animal Studies

The following 6 animal studies are presented chronologically. In general they show that tumors were produced following dermal exposure to creosote. As with coal tar, the Working Group notes that the interpretation of some of the early studies is limited by the absence of control data. However, later studies which include appropriate control groups generally confirm and reinforce the observations in the early studies.

(1) Sall and Shear

Sall and Shear (1940) reported on several experiments which tested the potential of the basic fractions of creosote to accelerate tumor production by known carcinogens. Female Strain A mice obtained from the Roscoe B. Jackson Memorial Laboratory in Bar Harbor, Maine, were used in all the experiments which included administration by skin painting and subcutaneous injection. In the skin painting experiments a mixture of 1% basic creosote and either 0.02% or 0.05% benzo[a]pyrene was applied three times per week to the treated animals. Concentrations of benzo[a]pyrene, at 0.02% and 0.05% were used alone for two control groups; another control group was painted with 1% basic creosote alone. There were no control groups in which healthy animals were used for comparison. The results of the skin painting experiments indicated that the basic fraction of creosote accelerated the tumor formation when applied with either 0.02% or 0.05% benzo[a]pyrene concentration, although the basic creosote alone produced no tumors. The results of the intramuscular experiment are not discussed here because intramuscular injection is not a route of exposure included in the criteria of 40 CFR 162.11(a)(3)(ii)(A).

(2) Woodhouse

Woodhouse (1950) studied the carcinogenic activity of 16 petroleum fractions and extracts, anthracene oil, creosote oil, linseed oil, pine tar, and six spindle oils dermally applied to 50 groups of ten-week-old, albino mice (undefined strain). Each test substance was applied with glass rods to the intrascapular area twice weekly for 25 weeks. Males and females were tested in approximately equal numbers. The animals surviving 25 weeks in each test group were counted, and papillomas and carcinomas were identified. Of the creosote-treated animals, 19 survived 25 weeks; 19 tumors (10 papillomas and 9 carcinomas) were reported. This was the highest number of tumors in the 10 treatment groups tested. There was no control group.

(3) Lijinsky et al.

A study by Lijinsky et al. (1956) evaluated creosote and its basic fracton as possible tumor-promoting agents. The experiment failed to demonstrate that creosote acts as a strong promoter when administered to mice receiving a single painting of 7,12-dimethylbenz[a]anthrancene (DMBA), but it did demonstrate that creosote is independently carcinogenic.

The creosote used was a "#1 oil, dry point 240° C, collected as a distillation fraction from a Wilton still." The basic fraction was prepared by the procedure of Cabot et al. (1940). Treatments were given twice weekly for 70 weeks to four groups of 30 female Swiss mice. A single drop of the treatment solution was applied with a glass dropper to the intrascapular region of the skin, which was kept free of hair by clipping with scissors. A control group (Group 1) consisting of 50 mice was treated with the initiating agent, 7,12-dimethylbenz[a]anthrancene (DMBA) given as a 1% solution in mineral oil. Group 2 was painted with undiluted creosote. The three remaining groups received a single initial painting of 1% DMBA in mineral oil; one week later they were treated with undiluted creosote (Group 3), 10% creosote in acetone (Group 4), or a 2% basic fraction of creosote solution in acetone (Group 5). There were no control groups in which healthy animals were used for comparison.

The tumor incidence in the five groups is shown in Table 16. The survival rate of the control animals given DMBA alone was not given; whatever their number, none of them were reported to have developed tumors.

TABLE 16

SKIN TUMOR INCIDENCE IN MICE TREATED WITH CREOSOTE
Carcinogen Assessment Group (CAG), 1977

Group	Initial Painting	Twice Weekly Painting	Incidence of Tumor-Bearing Mice 1/	Nos. of Papillomas	Nos. of Carcinomas	Average Latent Period (weeks)
1	1% DMBA	None	0/50 (0%)	0	0	0
2	None	Creosote: undiluted	13/26 (50%)	7	16	50
3	1% DMBA	Creosote: undiluted	17/23 (74%)	6	26	39
4	1% DMBA	Creosote 10% in Acetone	11/29 (38%)	7	8	43
5	1% DMBA	Creosote: 2% Basic Fraction	0/12 (0%)	0	0	0

1/ In group 1 there were 50 animals initially. In groups 2, 3, and 4 the denominator is the number of survivors at time of appearance of first tumor. In group 5 there there were 12 survivors at 56 weeks.

In contrast, there was a high tumor rate for animals pre-treated with DMBA and then treated repetitively with either undiluted or 10% creosote. Some enhancement of the action of a single initiating dose of DMBA was noted when given with undiluted creosote (50% vs. 74%), although the difference was not significant. Dilution of the creosote to 10% in acetone diminished the tumor producing action of DMBA plus creosote, while the basic fraction did not prove to be oncogenic.

In a companion study (Lijinsky et al., 1956) the creosote was chemically analyzed for benzo[a]pyrene, but less than 100 mg of benzo[a]pyrene was found per liter of creosote, an amount the authors consider too small to account for the carcinogenic activity of creosote. They suggested that some of the carcinogenic activity may result from the presence of benz[a] anthracene which was found in a relatively large quantity (2.75 gm/liter).

The results of this study showed that undiluted creosote alone produced a carcinogenic effect which was slightly augmented by the initial DMBA treatment. When the creosote was diluted to 10% the promoting action was somewhat diminished in relation to the undiluted creosote. The basic fraction of creosote at a 2% strength was inactive. The authors reported that the carcinogenic potential of the undiluted creosote was comparable to results found with DMBA, a potent carcinogen, in a similar test conducted at the same laboratory.

(4) Poel and Kammer

Poel and Kammer (1957) tested two "creosote oils" for carcinogenic potential on male and female mice. In the introduction to their report, Poel and Kammer described the difference between the definitions of coal tar fractions as they are classically defined and coal tar fractions as they are industrially used:

> The crude industrial fractions distilled from high-temperature coal tars are designated light oil, middle oil or napthalene crude cut, heavy creosote oil, anthracene oil and pitch (Table 17). A clear cut separation of tar into these distinctive fractions is usually not practiced on an industrial scale. In fact, such terms as creosote, heavy oil, and anthracene oil have been used synonymously, while certain industries to this day designate some pitches as "tars". Most of the marketed oil products are blends or smears, containing both creosote and anthracene oils plus varying amounts of the residual fractions from the middle-oil cut - the fraction shown in Table 17 to have a boiling range of 200 to 250°C.

The two "creosote oils" used in the study were described by Poel and Kammer as follows:

> Both are fractions from a high-temperature horizontal by-product-coke-oven tar. One is a crystal-free oil, marketed as a blend of creosote, anthracene oils, and the oil drained from the naphthalene recovery operation. This blend of oils has been described as nontoxic to humans and is used principally for the preservation of wood.... The second sample, considered a light creosote oil industrially [Table 17] is the residual oil drained from the naphthalene recovery operation.

The blended sample was tested in toluene at two dilution levels, 20% and 80%; the light creosote oil was tested at a 50% dilution in toluene. As a positive control, benzo[a]pyrene was tested in toluene at two dilution levels, 0.05% and 0.25%. Toluene was tested as a negative control.

The test animals were C57L mice, females, 10 to 12 weeks old and males 8 to 11 weeks old. The test solution was applied three times per week on the shaved back of each mouse for its lifespan or until persis-

TABLE 17

CRUDE COAL TAR DISTILLATES (POEL AND KAPPER, 1957)

Industrial Cut	Approximate Distillation Range (°C)	Fraction Recovered From Tar (%)	Principal Components of Fraction
Light Oil	200	5	Benzene, Toluene, Xylene, Solvent Naphtha
Middle Oil	200–250	17	Tar Acids, Tar Bases, Naphthalene, Light Creosote oil (residue)
Creosote Oil (Heavy)	250–300	7	Methylated Naphthalenes, Acenaphthene
Anthracene Oil	300–350	9	Fluorene, Phenanthrene, Anthracene, Carbazole
Pitch	> 350	62	Pitch Oil, Carbon

tent papillomas developed at the application site. Results of the test are found in Table 18.

These results show a significant increase in tumor incidence after topical treatment with both concentrations of blended creosote as compared to the incidence produced by the toluene control. All mice exposed to both dilutions of the blended creosote oil developed papillomas, and 7 of the 8 in each dilution group developed carcinomas. Among the creosote-treated animals that developed carcinomas, 5 of 14 had metastatic growths in the lungs and/or the regional lymph nodes. The 50% solution of light creosote oil in toluene produced tumors in all 11 male C57L-mice tested, after exposure ranging from 22 to 41 weeks. It was not reported whether the tumors were malignant or not. The presence of benzo[a]pyrene was tested for in light creosote oil and in the anthracene fraction of the blended creosote oil (where it most likely would be found). Detectable levels were not observed, and the authors concluded that the tumor response seen was due, at least in part, to other agents.

In summary, dermal application of light and blended creosote oils from high-temperature-coke-oven-tars induced significant increases in skin tumors on mice. Most of the tumors from the blended oil were carcinomas.

(5) Boutwell and Bosch

In a study which evaluated the tumor initiating and promoting activity of several chemicals, including creosote, and the carcinogenic potential of creosote without the use of initiating or promoting agents, Boutwell and Bosch (1958) found that creosote was carcinogenic when ap-

TABLE 18

TUMOR INDUCTION IN C57L MICE TREATED WITH BLENDED CREOSOTE, LIGHT CREOSOTE, BENZO[a]PYRENE, AND TOLUENE[1]

Test Material	Conc. in Toluene(%)	No. Mice with Tumors	No. Mice with Epidermal Cancer	No. Mice with Metastasis
Creosote Blend	80	8/8 (100%)[2]	7/8 (88%)[3]	3
Creosote Blend	20	8/8 (100%)[2]	7/8 (88%)[3]	2
Light Creosote	50[5]	11/11 (100%)[4]		
Benzo[a]pyrene	0.25	8/8 (100%)[2]	8/8 (100%)[2]	2
Benzo[a]pyrene	0.05	8/9 (89%)	7/9 (78%)	1
Toluene Control	0.0	0/10 (0%)	0/10 (0%)	0

1/ Female C57L mice were used in all groups except light creosote which used males.

2/ Significantly higher than controls ($p = 2.3 \times 10^{-5}$).

3/ Significantly higher than controls ($p = 2.5 \times 10^{-4}$).

4/ Significantly higher than controls ($p = 2.8 \times 10^{-6}$).

5/ The light creosote oil was administered as one drop of 50% (in toluene) creosote oil along with one drop of toluene.

plied to mouse skin, and that it had the ability to initiate tumor formation when applied for a limited period prior to treatment with croton oil. The mice used in the test were 8-week old, random-bred female albino mice.

The creosote was tested at full strength as obtained from Barrett Chemical Company. The trade name of the oil is Carbasota. It is described as "fractions distilled from a high temperature coke-oven-tar in the boiling range of 200 to over 400°C." Croton oil and DMBA used in the study were dissolved in re-distilled benzene. Solutions were protected from exposure to light and evaporation.

The solutions were applied as a 25 ul drop to the shaved skin of the back. Mice were inspected for tumors weekly and papillomas larger than 1 mm in diameter were counted. The gross identification of both benign and malignant tumors was confirmed periodically by microscopic examination.

There were 30 female mice in each group. The group applications were as follows: (Group 1) one drop (25 ul) of undiluted creosote twice-weekly with no initial treatment; (Group 2) one application of 75 ug DMBA followed (one week later) with 25 ul of benzene twice-weekly; (Group 3) single applications of DMBA as in Group 2, followed after one week with twice-weekly applications of 25 ul undiluted creosote; (Group 4) same initial treatment as in Groups 2 and 3 but followed with twice-weekly applications of 25 ul of a 0.5% croton oil in benzene solution; (Group 5) croton oil alone with no pre-treatment; (Group 6) undiluted creosote twice-weekly for four weeks only with no secondary treatment; (Group 7) undiluted creosote twice-weekly for four weeks followed with croton oil as in Groups 4 and 5. There were no controls in which healthy animals were used for comparison. The length of observation of each group was determined by the carcinogenic response (Table 19).

Papillomas and carcinomas developed in all groups given creosote except Group 6, where the duration of treatment may not have been long enough. Comparison of the results from Groups 6 and 7 show that creosote can act as an initiating agent prior to the application of croton oil. Pre-treatment with DMBA slightly reduces the induction time of tumors produced by repeated continuous creosote administration.

(6) Roe et al.

Roe et al. (1958) found that animals receiving dermal applications of creosote developed tumors of the skin and the lungs. The study consisted of two experiments. Two to three-month old mice were obtained from a commercial breeder for the first experiment. Prior to treating with creosote, the authors observed a total of 788 lung adenomas on the lobe surface of the lungs of 138 mice (an average of 5.8 adenomas per mouse) at 6-8 months of age. Since the commercial breeder had used creosoted wooden boxes to house the animals, it was determined that the lung adenomas were the result of housing the animals in these boxes. Some of these mice were allowed to breed in steel cages in the laboratory. The resulting progeny were found to have an average of only 0.5 adenomas per animal. Two groups of the fourth generation of the original mice were used in the first experiment. One group was bred in stainless steel cages and 24 of the resulting progeny (Group 1) were kept as untreated controls for eight months. Twenty-five progeny (Group 2) were treated twice-weekly

TABLE 19

SCHEDULE OF TREATMENTS AND TUMOR INCIDENCE IN MICE EXPOSED TO DMBA AND CREOSOTE

Group	Initial Treatment	Secondary Treatment (2x/wk)	Period of Treatment and Observation (wks)	Induction Time Carcinomas (wks)	Incidence of Carcinomas (%)[1]
1	None	Creosote	28	26	82[2]
2	75 ug DMBA	Benzene	56		
3	75 ug DMBA	Creosote	28	23	82[2]
4	75 ug DMBA	Croton Oil	54	36	80[3]
5	None	Croton Oil	44		
6	Creosote, 4 weeks, (2x/wk)	None	44		
7	Creosote, 4 weeks, (2x/wk)	Croton Oil	56	44	46[4]

---

[1] For groups 1,3,4, and 7, only percentages were reported; no carcinoma percentages were reported for Groups 2, 5, or 6.

[2] This incidence was recorded at 28 weeks.

[3] This incidence was recorded at 42 weeks.

[4] This incidence was recorded at 44 weeks.

on the backs with one drop (25 ul) of creosote oil (Carbasota) from the age of three weeks until six months and were observed for two months longer. The Carbasota was produced by the Barrett Chemical Company and was described as "a material in the boiling range of 200°C to over 400°C distilled from a high temperature coke-oven-tar." Progeny from the second group of the fourth generation mice were bred in wooden cages which were "thoroughly impregnated with creosote oil." They produced 29 young (Group 3). Group 3 mice were kept in the cages for the duration of the experiment and were treated for five months with one drop (25 ul) of creosote oil (Carbasota) applied twice-weekly after which they were kept for three months without treatment. After eight months Group 1 had an average of less than 0.5 adenomas per mouse. Group 2 had almost six per mouse and Group 3 almost 11 per mouse (Table 20, Experiment 1). Groups 2 and 3 together totaled 53 mice. Of this number, 5 bore skin tumors but no lung tumors; nine had lung tumors but no skin tumors; and 39 bore both skin and lung tumors. The incidence of skin and lung tumors in the controls was not given; therefore, a statistical analysis of the control versus the experimental groups is not possible. However, the total number of lung adenomas in Groups 2 and 3 was greatly increased over those of the controls (Group 1).

In the second experiment, random-bred albino mice were obtained from a supplier who used only metal cages for breeding. The control group (Group 1) of 50 animals consisted of two groups from a related study (Boutwell and Bosch, 1958), in which one group was treated initially with 75 ug of DMBA followed by a twice-weekly application of 25 ul of a 0.5% solution (w/v) of croton oil in benzene; and the other group

TABLE 20

THE EFFECTS OF CREOSOTE TREATMENT ON THE INCIDENCE OF LUNG ADENOMAS (Carcinogen Assessment Group, 1977)

Experiment	Group	Treatment	No. of Mice	Adenomas on Lung Surfaces	Adenomas per Mouse
1	1	None (control)	19	9	0.5
	2	One drop of creosote 2 times/week for 23 weeks	24	139	5.8
	3	One drop of creosote 2 times/week for 19 weeks in creosoted Cages	29	315	10.8
2	1	Initial treatment with 75 ug of DMBA followed by one drop of croton oil or benzene 2 times/week for approximately 55 weeeks (control)	50	15	0.3
	2	One drop of creosote 2 times/week for 4 weeks.	23	37	1.6

was treated initially with 75 ug of DMBA followed by a twice-weekly application of 25 ul of benzene. No untreated controls were used. The test group of 30 animals (Group 2) was treated twice-weekly for four weeks nine times) with one drop (25 ul) of creosote oil and thereafter kept under observation without further treatment. At 10 months 15 adenomas were seen in the 50 survivors of Group 1. On the other hand, the 23 survivors of Group 2 bore a total of 37 lung tumors (Table 20, Experiment 2). No skin tumors were reported for any of the mice in Experiment 2.

4. Coal Tar Neutral Oil

No human studies were found on coal tar neutral oil. The following three animal studies on coal tar neutral oil are presented chronologically.

(1) Cabot et al.

Cabot et al. (1940) painted albino "market" mice with benzene solutions of various creosote oil fractions together with benzo[a]pyrene. The fractions of creosote were prepared from a creosote oil obtained from a vertical-retort coal tar; 90% of the creosote oil distilled between 160^{o} C and 300^{o} C (Fraction 1). The basic constituents were first removed from creosote with aqueous hydrochloric acid (Fraction II); the phenols were removed with aqueous sodium hydroxide (Fraction III). The remaining neutral material (Fraction IV) was steam distilled, producing "neutral distillate" or neutral oil (Fraction V), and leaving the "neutral residue " (Fraction VI). The six fractions were dissolved in benzene containing either 0.2% or 0.05% benzo[a]pyrene. These solutions were painted on groups of 20 mice three times weekly for 20 weeks. Thereafter, the solutions containing 0.2% benzo[a]pyrene were applied twice-weekly for six additional weeks. With the solutions containing 0.05% benzo[a]pyrene, the the painting was continued three times per week for an additional 18 weeks. When a papilloma appeared, painting was continued until the skin growth attained an average diameter of about 4 millimeters. Control groups were painted with benzene solutions containing either 0.2% or 0.05% benzo[a] pyrene. No untreated controls were used.

Skin tumors occurred sooner and with greater incidence in animals tested with the high benzpyrene concentration than with the low concentration treatments. Four of the fractions had lower rates of tumor formation than the rates produced by benzo[a]pyrene alone. These four fractions were the parent creosote mixture, the phenolic fraction, the concentrated neutral distillate, and the neutral residue. The authors attributed the inhibitory effect of all but the phenolic fraction to skin damage, but suggested further experiments on the inhibition mechanism of phenolic fractions. Of the two promoting fractions, only the basic fraction had an enhancing effect at both benzo[a]pyrene concentrations.

(2) Berenblum and Schoental

Berenblum and Schoental (1947) extracted a horizontal-retort gas tar 1/ with light petroleum, then removed basic and acidic constituents by shaking with dilute HCl followed by dilute NaOH. The remaining neutral

---

1/ Although gas tar is made from coal, it is somewhat different from bituminous coking operation coal tar which is used for pesticide production in the United States. The Working Group, however, decided that the physical and chemical characteristics of the two are similar enough to make the results of this study relevant.

fraction was chromatographed and five coal tar neutral oil fractions were separated:

I. All bands up to and including anthracene
II. After anthracene, before benzo[a]pyrene
III. Benzo[a]pyrene bands
IV. Fluorescence bands 391, 412, and 430 mu
V. Fluorescence bands at 385 mu, and residue

The fractions were tested dermally on groups of 10 mice and 5 rabbits, for periods of 17-26 weeks, and were applied once a week on mice and twice a week on rabbits. No untreated controls were used. Fraction II was oncogenic to rabbits (5/5), but not to mice (0/11), Fractions III and IV were oncogenic to both rabbits (5/5 and 4/5, respectively) and mice (7/10 and 3/10, respectively). Fraction V did not produce tumors in mice or rabbits. The results of Fraction I were not reported. None of the crystals obtained from any of the fractions were oncogenic to mice or rabbits, which suggested that the oncogenicity of the fraction remained in the mother liquor.

(3) Horton

As discussed earlier, Horton (1961) evaluated the carcinogenic potential of coal tar and several coal tar fractions including coal tar neutral oil. In separating the coal tar fractions, coal tar acid was extracted with a 9% aqueous solution of sodium hydroxide from filtered benzene solutions of two different coal tars. The raffinates from this sodium hydroxide extraction of the tars were mixed with celite, agitated with concentrated HCl, and then filtered. The tar bases remained on the celite as solid hydrochlorides. The tar fractions from which the acids and bases had been removed were subjected to repeated contact with maleic anhydride in benzene solution at 60°C to extract the neutral anthracene-type of hydrocarbons (the neutral oils). The adducts formed with maleic anhydride were mixed with powdered soda-lime, and the neutral oil was regenerated by short path distillation at a dull red heat at atmospheric pressure. The remaining residue after extraction of the tar acids, the tar bases, and the neutral oil hydrocarbons was called the residual tar. The tar acids and the tar bases were dissolved in benzene at a concentration equivalent to their concentrations in the original coal tar. The maleic anhydride fraction (the neutral oil) was tested in a 1% solution of benzene. The residual crude tars were tested at 100% concentration; in addition, one of the crude tars was tested at a 50% concentration in benzene.

Ten-mg doses of the two coal tars and the diluted coal tar were dermally applied twice-weekly to mouse skin (the number and strain of mice tested was not stated), and 10-mg doses of the fractions and residual tars were applied three times per week. No untreated controls were used. The time of the tumor appearance was noted, and the relative carcinogenic potency of the different test substances was calculated on the basis of differences in time-to-tumor. This index was referred to as the potency for a minimum concentration of material (PMC). A high PMC value means a greater carcinogenic potency. Skin tumors appeared most quickly from the residual and crude tars: 24.8 and 23.6 weeks and 18.4 and 13.4 weeks from their respective residual tars. No tumors were reported from the acidic fractions of either tar. The basic fractions of the two tars produced tumors in 48.6 and 40.6 weeks, respectively, and the coal tar neutral oils (maleic anhydride extracts) from the two tars produced tumors in 34.1 and 32.1 weeks. The PMC values indicated that the residual and crude tars were most carcinogenic, with calculated values of 0.14 and 0.22 for the residual tars and 0.13 and 0.14 for the crude tars. PMC values for the coal tar neutral oils were 0.05 and 0.06; the PMC values for the basic fractions were 0.03 and 0.04. Since no tumors were produced by the acidic fractions, PMC values were not calculated.

5. Conclusion

a. Coal Tar

Shambaugh (1935), Mauro (1951), and Rosmanith (1953) reported on fishermen and net loft workers, tar distillery workers, and a tar worker, respectively, who had been occupationally exposed to coal tar and who had developed skin cancer. In animal studies, dermal application of coal tar produced skin tumors with mice [Horton (1961), Shabad et al. (1971), Watson and Mellanby (1930), Tsuitsui (1918), Hueper and Payne (1960), Deelman (1962), Bonser and Manch (1932), Gorski (1959), and Kennaway (1925)], and rabbits [Yamagiwa and Ichikawa (1915)]. Inhalation exposure to coal tarr produced lung tumors in mice [Horton (1961), MacEwen et al. (1976), Horton et al. (1963), and Tye and Stemmer (1967)], and rats [MacEwen et al. (1976)]. Exposure of mice to coal tar aerosol also produced skin tumors (McConnel and Specht, 1973; and MacEwen et al. 1976).

Horton (1961) found a dose response for skin tumors in mice following dermal application of coal tar. McConnell and Specht (1973) and

MacEwen and Vernot (1976) found a dose response for skin tumors in ICR-CF1 mice following inhalation exposure to coal tar aerosol. Horton (1961) and McConnell and Specht (1973) also found that the time-to-tumor was dose-related.

The Working Group concludes that coal tar produced tumors in three species of animals: mice, rats, and rabbits; that tumor response and time-to-tumor in the Horton (1961), McConnell and Specht (1973), and MacEwen and Vernot (1976) studies were dose-related; and that workers occupationally exposed to coal tar developed tumors. The Working Group thus concludes that coal tar is an oncogen and that it exceeds the criteria of 40 CFR 162.11(a)(3)(ii)(A). Accordingly, the Agency is issuing a rebuttable presumption against all pesticides containing coal tar.

b. Creosote

Henry (1947), Lenson (1956), O'Donovan (1920), Cookson (1924), and Mackenzie (1898) described various kinds of workers who were occupationally exposed to creosote and developed skin tumors. Dermal application of creosote produced skin tumors in mice [Woodhouse (1950), Poel and Kammer (1957), Lijinsky et al. (1956), Boutwell and Bosch (1958), and Roe et al. (1958)]. Roe et al. (1958) also found that dermal application of creosote to mice produced lung tumors. Boutwell and Bosch (1958) found that creosote had the ability to initiate tumor formation when applied for a limited period prior to treatment with croton oil. Sall and Shear (1940) found that the number of skin tumors was increased by dermal treatment with creosote and benzo[a]pyrene over the number of tumors produced by benzo[a]pyrene or creosote alone. The Working Group concludes that creosote produces tumors in mice; that creosote, when applied dermally, is a tumor-initiating agent when followed by dermal treatment with croton oil (Boutwell and Bosch, 1958); that creosote accelerates the tumor production caused by benzo[a]pyrene (Sall and Shear, 1940); and that workers occupationally exposed to creosote developed tumors. The Working Group concludes that creosote is an oncogen and exceeds the criteria of 40 CFR 162.11 (a)(3)(ii)(A). Accordingly, the Agency is issuing a rebuttable presumption against all pesticides containing coal tar.

c. Coal Tar Neutral Oil

Horton (1961) found that dermal application of coal tar neutral oil to mice produced skin tumors. Berenblum and Schoenthal (1947) found that several chromatographic fractions of coal tar neutral oil produced skin tumors when dermally applied to mice. Cabot et al. (1940) found that mixtures of coal tar neutral oil with benzo[a]pyrene decreased the number of tumors produced by benzo[a]pyrene alone, but suggested that this inhibiting effect was due to skin damage. The Working Group concludes that coal tar neutral oil produces tumors in mice, and that as an oncogen, it exceeds the criteria of 40 CFR 162.11(a)(3)(ii)(A). Accordingly, the Agency is issuing a rebuttable presumption against all pesticides containing coal tar neutral oil.

B. Mutagenicity

40 CFR 162.11(a)(3)(ii)(A) provides that "a rebuttable presumption shall arise if a pesticide's ingredient(s), metabolite(s), or degradation product(s)... induces mutagenic effects, as determined by multitest evidence."

In determining that this criteria was exceeded, the Working Group considered reports by Simmon and Poole (1978) and Mitchell and Tajiri (1978) who examined a creosote mixture of American Wood Preservers' Association (AWPA) specification P-1 and a coal tar-creosote mixture of AWPA specification P-2, Class C. The AWPA specifications for P-1 and P-2, Class C, are found in Appendices A and B. P-1 creosote is used for foundation piles, fresh-water piles, telephone poles, utility poles, fence posts, and other land and fresh-water uses. Class C P-2 coal tar-creosote is used primarily for railroad ties (Gibb, 1978c). *In vitro* microbiological assays with four strains of *Salmonella typhimurium*, TA 1535, TA 1537, TA 98, and TA 100, and *Escherichia coli* WP2 (Simmon and Poole, 1978) and *in vitro* mammalian cell bioassays with L5178Y mouse lymphoma cells (Mitchell and Tajiri, 1978) were conducted on both of the coal tar-creosote mixtures.

1. Simmon and Poole

Simmon and Poole (1978) conducted *in vitro* microbiological mutagenic assays on P-1 and P-2 using *Salmonella typhimurium* and *Escherichia coli* strains. These microbiological assays were conducted both with and without metabolic activation. Metabolic activation was provided by use of an Arochlor 1254-stimulated rat liver homogenate. Metabolic activation provides metabolic steps that the bacteria either are incapable of conducting or do not carry out under the assay conditions.

The Salmonella strains used were all histidine auxotrophs. They included: Strains TA 1537 and TA98 which are sensitive to frameshift mutations, TA 1535 which is sensitive to base-pair substitutions, and TA 100 which is sensitive to base-pair substitutions and some frameshift mutations. The *E. coli* WP2 strain is a tryptophan auxotroph and is sensitive to base-pair substitutions. The results of the mutagen tests on P1 and P2 are found in Table 21.

Except at the higher doses which were toxic, creosote P1 and coal tar-creosote P2, Class C, when metabolically activated, demonstrated a mutagenic dose-response and a doubling over the background level in the bacterial assay with Salmonella typhimurium strains TA 1537, TA 98, and TA 100. S. typhimurium strain TA 1535 and E. coli strain WP2 did not demonstrate a positive mutagenic response with metabolic activation. None of the strains demonstrated a positive response without activation. The fact that a mutagenic dose-response was found in the TA 1537, TA 98, and TA 100 S. typhimurium strains indicates that the mutagenic mode of action of the creosote and the creosote-coal tar mixture is by frameshift mutation.

2. Mitchell and Tajiri

Mitchell and Tajiri (1978) tested creosote of AWPA specification P1 and a coal tar-creosote mixture of AWPA specification P2, Class C, for mutagenic activity on an in vitro mammalian mutagenesis assay using L5178Y mouse lymphoma cells heterozygous at the thymidine kinase (TK) locus. The purpose of the test was to determine the effects of the P1 and P2 mixture on the forward mutation frequency of the TK locus, $TK^{+/-} \longrightarrow TK^{-/-}$, relative to the background level. Similar to the microbial assay described above, the mouse lymphoma study was conducted both with and without metabolic activation using an Arochlor 1254 stimulated rat liver homogenate mixture.

The mouse lymphoma cells were grown in suspension culture. The

TABLE 21

IN VITRO ASSAYS SALMONELLA TYPHIMURIUM AND ESCHERICHIA COLI
(Simmon and Poole, 1978)

Sample	Metabolic Activation	Amount of Sample Added Per Plate (ug)	Average Number of Revertants Per Plate				
			S. typhimurium				E. coli
			TA1535	TA1537	TA98	TA100	WP2
Negative Control	-		25	8	27	136	47
	+		17	8	41	154	44
Positive Control							
9-Aminoacridine	-	100		671			
2-Anthramine	+	2.5	179		1017	1211	
	+	10					542*
Creosote P1	-	5*	28	6	17	142	39
	-	10	32	6	28	132	39
	-	50	37	5	25	123	42
	-	100	34	7	18	137	34
	-	250*	29	4	16	75	39
	-	500	T	4	16	T	37
	-	1000*		T	10		26
	-	5000*			T		T
	+	5*	12	11	52	212	45
	+	10	20	14	60	215	49
	+	50	19	22	119	304	48
	+	100	17	30	125	330	40
	+	250*	26	52	149	441	47
	+	500	12	50	172	156	58
	+	1000*	T	31	214	T	44
	+	5000*		T	T		T

---

* Indicates the results of just one experiment. All other data are the average of two assays conducted on separate days.

T = Toxic

TABLE 21
(continued)

IN VITRO ASSAYS SALMONELLA TYPHIMURIUM AND ESCHERICHIA COLI
(Simmon and Poole, 1978)

Sample	Metabolic Activation	Amount of Sample Added Per Plate (ug)	Average Number of Revertants Per Plate				
			S. typhimurium				E. coli
			TA1535	TA1537	TA98	TA100	WP2
Coal tar-Creosote P2, Class C	-	5*	31	4	31	106	37
	-	10	22	6	23	128	35
	-	50	28	3	23	119	45
	-	100	28	7	17	122	40
	-	250	21	6	15	70	43
	-	500	21	3	15	55	40
	-	1000	11	4	14	T	27
	-	5000	T	T	T		T
	+	5*	10	11	43	185	55
	+	10	16	23	62	186	61
	+	50	19	26	95	293	62
	+	100	20	37	147	347	49
	+	250	16	41	183	65	72
	+	500	15	58	163	196	59
	+	1000	8	40	145	T	49
	+	5000	T	T	T		T

---

* Indicates the results of just one experiment. All other data are the average of two assays conducted on separate days.

T = Toxic

P1 and P2 mixtures were dissolved in dimethylsulfoxide (DMSO) and were added to the cell cultures in varying test concentrations. A solvent control using 1% DMSO and a positive control using either dimethylnitrosamine (DMN) (in the presence of metabolic activation) or ethyl methanesulfonate (EMS) (in the absence of metabolic activation) were also tested. The cells were plated (duplicates of each exposure concentration, the solvent control, and the positive control were run) on a selective medium containing trifluorothymidine. The mutated cells grew on the medium; the cells which had not mutated did not grow.

Mutation frequency was calculated as the ratio of the number of mutant cells to surviving cells at each concentration of test chemical. The mean mutation frequency of the negative control samples was subtracted from the mutation frequency of each treated sample to give induced mutation frequencies. A relative total growth was determined for the controls and for each test concentration. The relative total growth is an expression of cell growth in relation to the negative control and is expressed as a percentage (Tables 22 through 25).

Creosote P1 and coal tar-creosote P2 had similar but not identical effects on the forward mutation frequency at the TK locus of L5178Y cells both with and without induced metabolic activation. In the presence of the Arochlor 1254-induced metabolic activation, a dose related increase in mutation frequencies above the spontaneous frequency was established for both P1 and P2. For P1 without metabolic activation, the only concentration that yielded a mutation frequency significantly above the spontaneous frequency was 0.96 x 10^{-2} %. However, the relative total

TABLE 22

MOUSE LYMPHOMA FORWARD MUTATION ASSAY OF CREOSOTE P1 IN THE ABSENCE OF INDUCED METABOLIC ACTIVATION (Mitchell and Tajiri, 1978)

Concentration (percent v:v)	Relative Total Growth (%)	Calculated Mutation Frequency (x 10^6)	Induced Mutation Frequency (x 10^6)
Solvent Control (1% DMSO)	108.4	40	—
	90.2	66	—
Positive Control (500 ug/ml EMS)	37.2	573	520
	52.1	663	610
0.980×10^{-2}	0.16	286	233
	0.03	422	417
0.686×10^{-2}	36.8	57	4
	40.3	82	29
0.480×10^{-2}	71.4	60	7
	55.3	55	2
0.336×10^{-2}	78.3	79	26
	76.9	77	24
0.235×10^{-2}	68.2	47	0
	—	—	—
0.165×10^{-2}	68.3	71	18
	79.6	75	22
0.115×10^{-2}	138.9	54	1
	94.1	62	9
0.081×10^{-2}	85.1	68	15
	71.9	56	3

TABLE 23

MOUSE LYMPHOMA FORWARD MUTATION ASSAY OF CREOSOTE P1 IN THE PRESENCE OF INDUCED METABOLIC ACTIVATION[1] (Mitchell and Tajiri, 1978)

Concentration (percent v:v)	Relative Total Growth (%)	Calculated Mutation Frequency (x 10^{6})	Induced Mutation Frequency (x 10^{6})
Solvent Control (1% DMSO)	97.4	101	—
	102.6	94	—
Positive Control (100 ug/ml DMN)	6.3	445	347
	10.8	282	184
3.00×10^{-3}	0.8	459	361
	1.0	398	301
2.40×10^{-3}	3.9	318	221
	4.4	305	207
1.92×10^{-3}	9.9	213	115
	12.9	222	124
1.54×10^{-3}	23.0	167	70
	21.3	185	87
1.23×10^{-3}	36.7	180	82
	43.3	140	42
0.98×10^{-3}	42.8	169	71
	43.1	174	76
0.79×10^{-3}	62.7	151	53
	74.5	141	43
0.63×10^{-3}	84.3	120	23
	77.9	128	30

---

[1] Arochlor 1254-induced rat liver S-9, batch IR-11.

TABLE 24

MOUSE LYMPHOMA FORWARD MUTATION ASSAY OF COAL TAR-CREOSOTE P2 IN THE ABSENCE OF INDUCED METABOLIC ACTIVATION (Mitchell and Tajiri, 1978)

Concentration (percent v:v)	Relative Total Growth (%)	Calculated Mutation Frequency (x 10^{6})	Induced Mutation Frequency (x 10^{6})
Solvent Control	108.4	40	—
(1% DMSO)	90.2	66	—
Positive Control	37.2	573	233
(500 ug/ml EMS)	52.1	663	417
0.980×10^{-2}	0.02	233	227
	0.01	—	—
0.686×10^{-2}	41.6	143	90
	32.9	176	123
0.480×10^{-2}	57.7	87	34
	63.2	79	26
0.336×10^{-2}	75.9	—	—
	70.7	65	12
0.235×10^{-2}	85.5	58	5
	—	—	—
0.165×10^{-2}	—	—	—
	60.3	93	40
0.115×10^{-2}	65.7	59	6
	67.5	61	8
0.081×10^{-2}	55.4	74	21
	66.8	52	0

TABLE 25

MOUSE LYMPHOMA FORWARD MUTATION ASSAY OF COAL TAR-CREOSOTE P2 IN THE PRESENCE OF INDUCED METABOLIC ACTIVATION 1/ (Mitchell and Tajiri, 1978)

Concentration (percent v:v)	Relative Total Growth (%)	Calculated Mutation Frequency (x 10^6)	Induced Mutation Frequency (x 10^6)
Solvent Control	97.4	101	—
(1% DMSO)	102.6	94	—
Positive Control	6.3	445	347
(100 ug/ml DMN)	10.8	282	184
3.00×10^{-3}	2.8	386	289
	1.9	370	273
2.40×10^{-3}	7.0	269	172
	5.8	338	240
1.92×10^{-3}	14.4	204	106
	16.1	236	139
1.54×10^{-3}	35.0	134	37
	36.7	190	92
1.23×10^{-3}	35.0	140	43
	36.3	147	49
0.98×10^{-3}	50.7	177	80
	56.9	152	55
0.79×10^{-3}	58.9	153	56
	77.8	117	20
0.63×10^{-3}	73.7	123	26
	75.9	121	23

1/ Arochlor 1254-induced rat liver S-9, batch IR-11.

growth was below 1%. For coal tar-creosote P2 without metabolic activation, two concentrations, 0.98×10^{-2} % and 0.686×10^{-2} %, yielded a mutation frequency significantly above the spontaneous frequency. Again, the relative total growth value at 0.98×10^{-2} % was below 1% survival. At 0.686×10^{-2} % the relative total growth value was approximately 35%.

3. Conclusion

Simmon and Poole (1978) found that following metabolic activation by Arochlor 1254-stimulated rat liver homogenate both the creosote P1 and the coal tar-creosote P2, Class C, produced a mutagenic dose-response and a doubling above background mutation rate with *Salmonella typhimurium* strains TA 1537, TA 98, and TA 100. Mitchell and Tajiri (1978) found that, following metabolic activation by Arochlor 1254-stimulated rat liver homogenate, creosote P1 and coal tar-creosote P2, Class C, increased the number of forward mutations at the thymidine kinase locus of L5178Y mouse lymphoma cells in a dose-related manner. The Working Group concluded that P1 and P2, Class C, caused mutations in *Salmonella typhimurium* strains TA 1537, TA 98, and TA 100, and in L5178Y mouse lymphoma cells. The Working Group, therefore, concluded that P1 and P2 are mutagenic in a multitest system and exceed the criteria of 40 CFR 162.11(a)(3)(ii)(A). Accordingly, the Agency is issuing a rebuttable presumption against creosote and coal tar-creosote mixtures.

C. Exposure

Although 40 CFR 162.11(a)(3)(ii)(A) does not require that exposure be demonstrated in order to presume against a pesticide on the basis of oncogenicity or on the basis of mutagenicity in a multitest system, a discussion of exposure to coal tar, creosote, and coal tar neutral oil is included for comment by interested persons. The Working Group considered three areas of exposure to these substances - industrial wood treatment, food residue, and user exposure.

1. Industrial Wood Treatment

a. General

The most important minor method of application is thermal treatment in which wood is immersed in open troughs filled with hot creosote followed by introduction of relatively cold creosote. The Working Group is not aware of any information on exposure to creosote from thermal treatment. The application of over 90% of all coal tar-creosote mixtures for wood preservation is by pressure treatment (American Wood Preservers' Institute, 1977).

The pressure treatment system is a closed system, and there is no need for direct worker contact with the liquid creosote or coal tar prior to its impregnation into the wood. The material arrives by truck or rail and is pumped into a holding tank where it is weighed. If the material is a creosote/coal tar solution of particular trade specifications, the solution is premixed at the production facility so that no mixing or manual transfer operations are required at the treatment plant. The treatment itself involves pressurization in airtight chambers. No workers are likely to be exposed from the treatment cylinders during the actual treatment process, nor are workers other than treating room operators required to be in the immediate vicinity of the chambers at this time. The treatment operator is responsible for the metering and introduction of coal tar/creosote into the cylinders. This function is performed in a control house near the chambers. In older facilities leakage of coal tar and creosote from old pipes and fittings may result in relatively high inhalation exposure to the treatment operators. Treatment time varies but ranges from about six to seven hours for each change of material. Following treatment, a vacuum is generally applied to withdraw excess preservative. After the excess is withdrawn, the chamber door is cracked open by a doorman. While still under vacuum, prior to withdrawal of the tram cars holding the treated wood, the door remains cracked open for approximately 15 minutes. The greatest opportunity for inhalation exposure appears to occur during the mechanical withdrawal of the tram cars from the pressure chamber. The wood-laden tram cars are linked to an engine and withdrawn to a storage area where the wood remains until shipment to the buyer.

Coal tar and creosote drippage occurs along the rail tracks leading from the chamber. This drippage is collected in ditches alongside the tracks and is pumped to a collecting pond along with creosote that has dripped from the pressure chambers at the time the charge was removed. Dike systems are employed around wood treatment plants to prevent runoff of creosote from the plant area. In at least one case, however, creosote was found to migrate from a treatment plant into the ground water supply of a neighboring community. The plant has since been shut down (Mittelman, 1978).

Non-routine operations such as cleaning of the treatment chamber may occur several times yearly. Workers in such operations are provided with suitable respirators and protective clothing.

b. Inhalation Exposure

On February 24-25, 1976, representatives of the National Institute of Occupational Safety and Health (NIOSH) [U.S. Department of Health, Education, and Welfare (USDHEW), 1977] and of Koppers Company (Smith, 1977) performed two separate air monitoring surveys at a Koppers Company wood preservation plant in Little Rock, Arkansas. Air samples were collected using lapel sampling pumps and analyzed for polycylic particulate organic matter (PPOM) by the NIOSH gravimetric method (NIOSH, 1977). The results of the two studies are presented in Table 26 and Table 27. [1]

Koppers Company also performed an air monitoring survey in July, 1977 (Webb, 1977) at the same Little Rock, Arkansas plant sampled by Koppers

---

[1] The lapel air sampling pumps collected the PPOM on a silver membrane-glass fiber filter which was held in place by a cellulose pad. Following collection of the air sample, NIOSH (USDHEW, 1977) desorbed the filter and the cellulose pad with cychlohexane. By contrast, Koppers (Williams, 1977) (Table 27) desorbed the filters, but not the cellulose pads, with benzene. The cyclohexane solution, or the benzene solution in the case of the Koppers' analyses, was placed in a teflon cup and the benzene or the cyclohexane was evaporated by placing the cup in a vacuum oven for three hours at 40°C. The weight of the remaining material was the cyclohexane or benzene soluble material. The concentration of mg/m^3 was determined by dividing the weight of the cyclohexane or benzene soluble material by the volume of air sampled. The results of the NIOSH analysis were generally higher than those of Koppers'. NIOSH, however, as stated above, desorbed the cellulose pad as well as the filter with cyclohexane, while Koppers desolved only the filter. Analysis of two blank cellulose pads for PPOM by NIOSH produced results of 115 and 120 ug/filter. No adjustment in the NIOSH report was made for the blank cellulose pads. To adjust for the blank samples, 117.5 ug/filter (the average of 115 and 120 ug/filter) was subtracted from the ug/filter reported for the NIOSH test samples by an EPA chemist for the purpose of presenting the table of results in this document. Where no results are reported for the "ug/filter" in Table 28, the ug/filter of the blank sample was higher than the test sample.

TABLE 26

RESULTS OF 1976 NIOSH MONITORING STUDY AT KOPPERS COMPANY WOOD TREATMENT PLANT IN LITTLE ROCK, ARKANSAS (U.S. Department of Health, Education, and Welfare, 1977)

Description (Date)	ug/filter[1]	Air Volume Sampled (m^3)	Concentration In Air (mg/m^3)[2]	Code of Worker or Site[3]
Treating Operator (2/24)	32.5	0.49	0.07	SM-6
Doorman (2/24)	-	0.53	-	SM-7
Treating Operator (2/25)	62.5	0.49	0.13	SM-11
Doorman (2/25)	-	0.51	-	SM-12
Locomotive Operator (2/24)	12.5	0.49	0.03	SM-8
Locomotive Operator (2/25)	52.5	0.56	0.09	SM-15
Locomotive Switchman (2/24)	-	0.73	-	SM-9
Locomotive Switchman (2/24)	-	0.57	-	SM-10
Locomotive Switchman (2/25)	137.5	0.50	0.28	SM-13
Locomotive Switchman (2/25)	42.5	0.50	0.08	SM-14
Treating Area[4]	52.5	0.44	0.12	SM-16

1/ This is the total amount measured on the filters minus the amount measured on the cellulose control blank.

2/ This is the concentration in the air of cyclohexane soluble polycylic particulate organic material.

3/ This code was given to each worker or site sampled. The same codes were used by Koppers Company in their sampling. See Table 27 for a comparison of the results.

4/ This is a stationary area sample. The other samples were collected from label sampling pumps.

TABLE 27

RESULTS OF 1976 KOPPERS' MONITORING STUDY AT KOPPERS COMPANY WOOD TREATMENT PLANT IN LITTLE ROCK, ARKANSAS (Smith, 1977)

Description (Date)	Concentration In Air (mg/m3)[1]	Code of Worker or Site
Treating Operator (2/24)	0.10	SM-6
Locomotive Switchman (2/24)	0.07	SM-9
Locomotive Switchman (2/24)	0.07	SM-10
Locomotive Switchman (2/25)	0.07	SM-15

---

[1] This is the concentration in the air of benzene soluble polycyclic particulate organic material.

TABLE 28

RESULTS OF 1977 KOPPERS COMPANY MONITORING STUDY AT LITTLE ROCK, ARKANSAS (Webb, 1977)[1]

Description	Concentration In Air (mg/m^3)[2]
Doorman	0.02
Doorman	0.07[3]
Treating Operator	0.05
Treating Operator	0.01
Switchman	0.03
Switchman	0.02
Switchman	< 0.01
Locomotive Operator	0.05
Locomotive Operator	0.01
Boring Operation	0.04
Area Clean Up	0.02

---

[1] The weather conditions during the study were the following: temperature, 72-83°F; relative humidity, 74-91%; barometric pressure, 30.00 inches Hg; and winds from the north at 5 mph.

[2] This is the concentration in the air of benzene soluble material.

[3] This doorman's exposure may have been higher because of his recovering a tram inside the cylinder following a break of the tram tow cable.

Company and NIOSH in July 1976 and using the NIOSH gravimetric technique used in the first Koppers' study. The results of the 1977 study are reported in Table 28.

The 1976 and 1977 Koppers' studies found a range of < 0.01 to 0.10 mg/m^3 benzene soluble material concentration in the air around the Little Rock wood treatment plant. The 1976 NIOSH study found a range of 0.03 to 0.28 mg/m^3 cyclohexane soluble material in the air around the Little Rock plant. No correlation appears to be evident between the type of work performed (e.g. treating operator, locomotive switchman, doorman, etc.) and the amount of air exposure.

There are several limitations to the method of collection employed by NIOSH. As stated, the method of analysis used is a gravimetric method and measures only the benzene or cyclohexane soluble fraction of polycyclic particulate organic matter in air samples. Thus, vapor phase polynuclear aromatic (PNA) hydrocarbons would go uncollected. Also, the gravimetric method used has not been fully evaluated for precision or accuracy nor has the solvent system been properly assessed for extraction efficiency. Another limitation to this method of analysis is its nonspecificity, i.e., the organic material weighed may include innocuous as well as carcinogenic materials.

c. Dermal Exposure

Handling of the treated wood at a pressure treatment plant is performed either mechanically or with metal utensils so that direct dermal exposure is minimal. Some dermal exposure does occur, however, as evidenced by reports of skin sensitization and burns, conjunctivitis, and eye irritation of workers in pressure treatment plants (McMillan, 1976).

2. Residues in Food

Creosote, coal tar, and coal tar neutral oil are not applied to food crops. Some evidence exists, however, that creosote or creosote-coal tar mixtures may leach out of marine pilings and contaminate marine life in the near vicinity and that this marine life may be eaten by humans or move through the food chain.

Dunn and Stich (1975, 1976a, 1976b) monitored mussel benzo[a]-pyrene contamination, and Zitko (1975) monitored various aquatic fauna for pyrene equivalents. Dunn and Stich (1975) found that mussels taken from a relatively pollution-free location contained higher benzo[a]-pyrene levels (49 ± 5.8 ppb) when near creosoted pilings than when distant from the pilings (2.1 ± 0.3 ppb). Analyses for the B[a]P was performed by thin layer chromatography (TLC) and fluorescent emission spectra. While TLC techniques have, for the most part, been superseded by high pressure liquid chromatography (hPLC) and gas chromatography (GC) methods offering greater separation from potential interferences and greater sensitivity, the data generated is valid and deserves greater investigation. Although it was not conclusively demonstrated that creosote was the source of the B[a]P contamination, it is not unlikely that creosote constituents may migrate from wood over time if only by purely mechanical means such as abrasion or swelling of the wood. The extent of this migration is unknown, but the data provided by Dunn and Stich (1975) must be considered in the absence of better-developed data.

The Working Group concluded that the extent of potential dietary exposure due to shellfish is unknown, but is likely to be small. A total of 3.73 g/day of fresh, frozen, and canned shellfish was consumed per capita in the United States in 1974 (USDA, 1974). If it is assumed that shellfish taken from sites near creosoted pilings contain approximately 50 ppb B[a]P (i.e. 50 ug/kg) (Dunn and Stich, 1975), then the maximum daily intake of B[a]P would be 50 ug/kg x 3.73 g = 0.19 ug/person/day B[a]P. This exposure would result only if all shellfish contained the B[a]P content detected by Dunn and Stich, an assumption without supporting data, and also assuming the data of Dunn and Stich is representative of all shellfish near creosoted pilings.

3. User Exposure

a. Use of Treated Wood

Schwartz (1942) reported that workers exposed to creosoted floors developed erythematous, papular, and vesicular eruptions on their ankles one to two weeks after beginning work. The Pesticide Episode Reporting System (PERS) (1976) reported a number of incidents in which workers handling creosote-treated wood suffered adverse effects from exposure to the creosote (Appendix C).

The Working Group concluded that exposure from the handling of treated wood by workers such as railroad workers, utility pole workers, and workers installing pilings deserved greater attention. When this work is done in the summer, workers would probably incur the greatest potential exposure because of the inconvenience and discomfort of wearing protective clothing during this time of year.

b. Manual Application of Coal Tar, Creosote, and Coal Tar Neutral Oil for Wood Preservation

Birdwood (1938) reported on the permanent damage to vision of two gardeners who had gotten creosote in their eyes while treating fences. Jonas (1943) reported that Navy construction workers developed skin and eye irritation as a result of exposure to creosote while applying the creosote during construction. The Pesticide Episode Reporting System (1976) reported a number of incidents in which workers applying creosote suffered adverse effects from exposure (Appendix D).

The Working Group concluded that applicators who manually apply creosote are exposed, but no information is available to quantify this exposure.

c. Application of Creosote as an Herbicide

The Pesticide Episode Reporting System reported two cases of burns to applicators applying creosote as an herbicide (Appendix E).

The Working Group concluded that exposure to creosote does result from its application as an herbicide. The Working Group, however, is not aware of any information that is available to quantify this exposure.

d. Other Uses

Coal tar neutral oil and creosote are active ingredients of two insecticides used on horse and mule wounds (2 registrations). Coal tar neutral oil and creosote are both active ingredients of disinfectants for water closets, outhouses, garbage cans, animal areas, institutional premises, and sickroom areas (approximately 57 registrations). Coal tar and coal tar neutral oil are active ingredients in pesticide dips and shampoos for dogs (approximately 7 registrations). Creosote is an active ingredient of a pesticide registered for mite and tick control in poultry houses. Coal tar neutral oil is an active ingredient of a pesticide registered for use on hog houses, sheep barns, dog kennels, and horse stables (6 registrations).

Creosote is an active ingredient in registrations for horse repellent (1 registration), a tree and shrub dressing (3 registrations), and an herbicide (2 registrations). Coal tar is an active ingredient in a crow repellent for seed corn (1 registration) and a human insect repellent (1 registration). Coal tar neutral oil is an active ingredient of approximately 16 mosquito larvicide registrations and 2 gypsy moth larvicide registrations.

No information is available regarding the potential exposure during application for the above uses. The uses involving coal tar and its derivatives in animal dips, washes or shampoos and the use of coal tar as a human insect repellent appear most likely to result in direct human contact.

III. OTHER ADVERSE EFFECTS

A. General

The information in this section relates to other adverse effects of creosote. The Working Group has concluded that the presently available information does not require issuance of a rebuttable presumption against registration on these effects. The Agency does solicit information on these problems, however, and requests that studies be conducted where necessary.

B. Skin and Eye Irritation

The Working Group reviewed several reports indicating that creosote is a potent skin and eye irritant.

Birdwood (1938) reported on two gardeners who got creosote into their eyes while creosoting fences. The two patients both complained of blurred vision and upon examination were found to have maculae upon the cornea and keratitis of the cornea. Birdwood reported that for both patients the impairment of vision would be permanent.

As indicated previously, the Pesticide Episode Reporting System (1976) reported 33 cases of eye damage, burns, or dermatitis resulting from creosote exposure either from treated wood or by application during the period August 1968 to April 1976 (Appendices C,D, and E).

McMillan (1976) reported on the accident history of 50 of the approximately 175 pressure-treating plants in the United States and Canada which use creosote to treat wood. About 3,000 employees out of approximately 7,000 employed in the industry were surveyed. Of those surveyed, 230 were reported to be directly exposed to creosote and fifteen hundred employees were reported to be either directly or indirectly exposed. The report was vague on the period of time which the survey covered. One employer reported for a 6-year period (1969-1975), one employer reported for a 10-year period (1961-1971), and 5 employers' reports were termed "historical." The time period covered for the other 43 plants was not reported. Also vague in the report was the number of treatment plants which documented or did not document the accident history. Of those which were documented, 98 cases of chemical conjunctivitis and 19 cases of eye irritation were reported. At least one treatment plant reported that eye irritation was "occasional." Sixty cases of skin burns and two allergic reactions were reported. At least one plant reported that skin burns were "infrequent."

Pfitzer et al. (1965) found that the instillation of 0.1 milliliter of creosote into the eyes of rabbits caused the conjunctiva to become slightly erythematous. Examination of the exposed eyes 24 hours following exposure showed that slight redness of the conjunctiva persisted in two of the eyes tested and the remaining four exposed eyes were essentially free of irritation. All of the exposed eyes were free of any apparent effects after seven days. Pfitzer et al. (1965) also reported that the contact of creosote with the intact and abraded areas of the skin of the bellies of rabbits for a maximum period of 24 hours produced moderate erythema and moderate to severe edema. The skin reactions remained relatively unchanged 72 hours following exposure. After 14 days, the exposed areas revealed severe epidermal flaking.

Schwartz (1942) reported that workers exposed to creosote treated floors developed erythematous, papular, and vesicular eruptions on their uncovered ankles one to two weeks after beginning work.

Jonas (1943) treated 450 Navy construction workers (1/6 of the workers at a Navy camp) for creosote burns. He found that fair-skinned, light-haired workers were particularly affected by creosote burns and that the number of burns increased on sunny days. Seventy percent of the burns were mild, while 30% were more severe and characterized by intense burning, itching, and considerable subsequent pigmentation followed by desquamation. Fifteen percent of the 450 patients had inflammation of the conjunctiva, with mild cases being characterized by hyperennia of the mucus membranes and more severe forms by photophobia and a large amount of serous secretion. Three percent had injuries to the cornea varying from small abrasions to multiple large ones. One-third of these cases developed permanent corneal scars leaving hazy vision. These injuries were caused by flying chips of creosoted wood.

C. Toxicity to Livestock

The Working Group reviewed several reports indicating that creosote may have been responsible for toxic effects and death in some livestock.

1. Hanlon

Hanlon (1938) reported the loss of four steers and two cows from a lot of 94 head of cattle from what appeared to be creosote poisoning. The cattle were believed to have licked electric light poles which had recently been creosoted. Symptoms in affected animals consisted of extremely rapid respiration and evidence of burning over the mucosa of the mouth, tongue and lips, which were white and hardened. The pupils were contracted, the skin was cold, and the animals were in a comatose condition. Feces were black in color and the affected animals were apparently in agony. In the early stages they were reported to have evinced great thirst. A steer *in extremis* was killed, and an autopsy carried out immediately. Intense inflammation and congestion was evident in the whole gastrointestinal tract.

2. Lander

Lander (1926) (cited in Hanlon, 1930 and harrison, 1959) reported the death of stock that had access to freshly treated railway ties. He stated that water may dissolve sufficient cresols from creosote-treated sleeper ties to cause livestock poisoning.

3. Wanntorp

Wanntorp (1953) (cited in Harrison, 1959) described several cases in which calves and cows died or had to be slaughtered after licking creosoted wood or poles. He mentions also the possibility that losses of poultry following the treatment of fowl houses with carbolineum (a high boiling point tar oil) may have been due to poisoning by tar derivatives.

4. Luke

Luke (1954) reported the death of four pigs, the suspected cause of which was the ingestion of coal tar pitch from the floor of their pen. The floor was made of old railway ties leveled off with pitch. Prior to death, the appetite of the pigs was very poor and coughing was widespread. Postmortem examination of the pigs found marked enlargement of the liver and several other liver anomalies in all four cases. Also, the abdominal cavities contained varying quantities of bloodstained fluid, and there was an excess of straw colored fluid in the pleural cavities. A pyogenic pneumonia was found in two carcasses, and in one of these there was a well-marked pericarditis. The lungs were normal in two cases and in one of these a marked cystic condition of the kidneys was found. C. pyogenes was isolated from the pneumonic lungs but cultures from liver, spleen, and heart blood were uniformly negative. From their findings, the authors concluded that pneumonia was not the principal cause of death, but that the death resulted from the liver damage. To test this hypothesis, the pitch was fed to two groups of healthy pigs. Group A was comprised of three healthy pigs, each about 60 pounds in weight, and Group B of two pigs, each about 40 pounds in weight. The pigs in Group B were not thriving quite as well as those in Group A. A quantity of pitch was ground up and a small quantity added daily to the food for both groups. Over a period of 28 days, Group A received a quantity of two pounds of pitch. The pigs in Group B received four ounces of pitch over a period of 12 days. In both groups the addition of the pitch affected appetite and the pigs tended to be constipated. At the end of feeding for both groups, the pigs were killed and examined. In all three cases from Group A the pigs showed an enlargement of the liver together with a degree of liver damage similar to those of the original cases. Extensive liver lesions and a marked excess of peritoneal fluid were found in the pigs of Group B. Histological examination of the affected liver tissue from both field and experimental animals showed similar changes, viz. a marked central necrosis of the lobules which in some cases had completly destroyed the normal liver cell.

5. Harrison

Harrison (1959) determined from his experimental data that a 30 kg sheep would have to ingest 300 g of wood or 120 g of creosote to receive an acutely fatal dose; a 100 kg calf would have to ingest 1,000 g of wood or 400 g of creosote for the dose to be acutely fatal. These acute lethal doses are not LD 50 values, however. A chronic fatal dose for sheep would be 37.5 g of wood or 15 g of creosote ingested per day over a 1 month period; a chronic fatal dose for calves would be 125 g or 50 g of creosote per day for at least 11 days. Harrison thought that the only danger to stock would be through their access to the raw preserving fluid either near stacks of freshly impregnated timber or on freshly treated farm timber and nearby contaminated vegetation.

6. Olafson and Leutritz

Olafson and Leutritz (1958) applied cresote to the skin of calves over the jaw area to preclude licking off the material. About three days after application, the skin developed slight swelling and became harder than normal. Gray creases appeared. From 7 to 10 days later, a dry crusty thickening of the skin had occurred. Healing took place slowly and recovery was not complete in four weeks.

Olafson and Leutritz (1958) also studied calf response following oral administration of creosote. They reported that a 1,000-pound cow would have to ingest over 75 cc of creosote before appreciable harm would result, although the exact basis for this determination was not stated.

D. Fetotoxicity

The Working Group identified one livestock study, the results of which may pose a question as to the fetotoxicity of creosote.

Schipper (1961) found a creosote-related fetotoxic effect with pregnant sows; the platforms of the cages in which the sows were housed had had three brush applications of a commercial creosote wood preservative.* The sows were confined in the cages 2 and 10 days before giving birth. Twenty-four of the forty-one pigs delivered by the four sows were dead at birth. Of the remaining offsprings, six pigs died on day 1, four pigs on day 2, and one pig on day 3. The surviving pigs had rough skin, were dehydrated, and had severe diarrhea; weight gains were hindered until they were 5 and

6 weeks old. A control group was not included in the study, and the author did not report the route nor the amount of exposure.

Appendix A

SPECIFICATIONS FOR COAL-TAR CREOSOTE (NEW MATERIAL) (Fuller, 1977)

SPECIFICATION NUMBER	P1-65(1)	P13-65(2)	D390-67(3)	TT-C-645b(4)		
				Class 1	Class 2	Class 3
Water (% by volume)	> 1.5	> 1.5	1.5 max	2.0 max	3.0 max	3.0 max
Matter insoluble in benzene (% by weight)	> 0.5	> 0.5	0.5 max	1.5 max	1.5 max	1.5 max
Specific gravity at 38° C compared to water at 15.5°C						
Original creosote	< 1.050	< 1.080	1.05 min	1.050 min	1.050 min	1.080 min
235-315°C fraction	< 1.027	< 1.030	0.027 min	1.027 min	1.027 min	1.030 min
315-355°C fraction	< 1.095	< 1.105	1.095 min	1.095 min	1.095 min	1.110 min
Residue above 355°C	–	< 1.160	–	–	–	1.160 min
Distillation						
To 210°C	> 2.0	> 2.0	2.0 max	2.0 max	2.0 max	2.0 max
To 235°C	>12.0	>12.0	12.0 max	12.0 max	12.0 max	12.0 max
To 270°C	<20.0;>40.0	20.0;>40.0	20.0-40.0	20-40	20-40	20-40
To 315°C	<45.0;>65.0	45.0;>65.0	45.0-65.0	45-65	40-65	45-65
To 355°C	<65.0;>82.0	65.0;>75.0	65.0-82.0	75-82	65-82	65-75
Service	Land, fresh water	Marine	Land, fresh water	Poles	General, land, fresh water	Marine

(1) For land and fresh water use. AWPA Std.
(2) For marine (coastal water) uses. AWPA Std.
(3) For land and fresh water use. ASTM Std.
(4) GSA standards for creosote in use.

Appendix B

AWPA SPECIFICATIONS OF CREOSOTE-COAL TAR SOLUTIONS (NEW MATERIAL)

(Fuller, 1977)

REFERENCE	AWPA P2-68 GRADE A	B	C	D	P12-68[1]
Composition					—
Creosote	<80	<70	<60	<50	—
Coal Tar	—	—	—	—	—
Water (% by volume)	> 3.0	> 3.0	> 3.0	> 3.0	3.0
Benzene, insol. (% by weight)	> 2.0	> 3.0	> 3.5	> 4.0	1.0-3.0
Coke residue (% by weight)	> 5.0	> 7.0	> 9.0	>11.0	4.0-7.0
Specific Gravity (38/15.5)					
Whole oil	1.06-1.11	1.07-1.12	1.08-1.13	1.09-1.14	1.090
235-315°C fraction	1.025	1.025	1.025	1.025	1.030
315-355°C fraction	1.085	1.085	1.085	1.085	1.105
Residue	—	—	—	—	1.185
Distillation					
To 210°C	5	5	5	5	5.0
To 235°C	25	25	25	25	15.0
To 270°C	—	—	—	—	20-35
To 315°C	36	34	32	30	35-50
To 355°C	60	56	52	48	55-70
Residue	—	—	—	—	—

(1) For use in treatment of marine piles and timbers.

Source: Hartford (1973).

APPENDIX C

REPORT OF EPISODES OF EXPOSURE TO CREOSOTE FROM TREATED LUMBER[1]

(Adapted from PERS, 1976)

Date of Episode	State	Causative Agent Verification[2]	Remarks[3]
2/25/73	CA	Probable	A dockworker developed a rash on his arms after contacting crates coated with creosote.
4/5/73	CA	Probable	A carpenter sustained chemical burns on his face, hands and arms while painting fence posts with creosote.
4/12/73	CA	Yes	A carpenter was handling timbers at a shipyard. Creosote splashed into his left eye, which developed redness and pain.
4/26/73	CA	Probable	A welder developed a rash on his hips, chest, thighs and trunk while working around treated railroad ties.
6/1/73	CA	Probable	A maintenance man developed an erythematous rash, first degree burns and chemical irritation while handling freshly treated poles.
6/29/73	CA	Probable	A wood worker developed first degree chemical burns when he rubbed the chemical on his face while working.
7/9/73	CA	Probable	An equipment operator for a county water agency was removing poles treated with creosote all day. His face and neck became red, swollen and sore.
8/9/73	CA	Probable	A lineman was holding treated utility poles with gloves when he wiped his face, thereby transferring creosote from the gloves to his face. Diagnosed as chemical burn.

APPENDIX C
(continued)

REPORT OF EPISODES OF EXPOSURE TO CREOSOTE FROM TREATED LUMBER[1]
(Adapted from PERS, 1976)

Date of Episode	State	Causative Agent Verification[2]	Remarks[3]
9/20/73	CA	Probable	Laborer developed contact dermatitis on his buttocks while working with treated lumber.
1/75	CA	Yes	Laborer working with treated wood developed dermatitis on hands and arms.

1/ Records checked from 1967 through April, 1976.

2/ Verification indicates whether the pesticide associated with the episode was established as the causative agent which resulted in death, illness, etc. "Yes" indicates that substantial evidence exists linking the pesticide to the episode's effects; "Probable" indicates circumstantial evidence exists linking the pesticide to the episode's effects.

3/ In all cases 1 human received medical attention.

APPENDIX E

REPORT OF EPISODES OF EXPOSURE TO CREOSOTE FROM APPLICATION [1]
(Adapted from PERS, 1976)

Date of Episode	State	Causative Agent Verification [2]	Remarks [3]
2/23/72	CA	Probable	A carpenter developed sub-acute conjunctivitis after getting creosote in his eye at work.
8/72	CA	Probable	A carpenter sustained burns of the face, arms and hands when he came into contact with creosote spray.
10/2/72	CA	Probable	A construction worker developed a rash on all extremities while working with creosote.
4/23/73	CA	Probable	A construction worker developed chemical burns of both forearms while carrying creosote-treated wood.
4/26/73	CA	Probable	A laborer at a lumber yard sustained first degree burns on both arms while moving creosote from a tank.
6/6/73	CA	Probable	A laborer developed erythema of the face, neck and forearms when he inadvertently rubbed creosote on them.
6/11/73	CA	Probable	A carpenter splashed creosote into both eyes and developed chemical keratoconjunctivitis.
6/18/73	CA	Probable	A carpenter spilled creosote on arms and face and developed superficial irritation of arms and face.
6/27/73	CA	Probable	A student got creosote on forearms while painting posts and developed chemical burn.

APPENDIX D
(continued)

REPORT OF EPISODES OF EXPOSURE TO CREOSOTE FROM APPLICATION[1]
(Adapted from PLRS, 1976)

Date of Episode	State	Causative Agent Verification[2]	Remarks[3]
7/24/73	CA	Probable	A laborer developed first degree burns of the arms, face and hands after painting posts with creosote.
7/26/73	CA	Probable	A carpenter sustained first degree burns on his face, forearms and lower abdomen when he splashed the material on himself during an application operation.
7/31/73	CA	Probable	A laborer for a construction company sustained a chemical burn when the material was sprayed on his arms and face.
9/24/73	CA	Probable	A laborer got creosote in his face and eyes thereby sustaining a chemical burn.
8/24/74	NJ	Yes	A woman was injured when the can from which she was pouring creosote onto the foundation of her home, slipped from her hand, splashing the chemical on her legs and into her eyes.
4/25/75	CA	N/A	A man was applying creosote to a ramp when he accidentally splashed it on his face. The effect of the accident was not reported.
5/25/75	CA	Probable	An employee was treating a wooden block. Material splashed onto him, resulting in contact dermatitis.

1/ Records checked from 1967 through April, 1976.

2/ Verification indicates whether the pesticide associated with the episode was established as the causative agent which resulted in death, illness, etc. "Yes" indicates that substantial evidence exists linking the pesticide to the episode's effects; "Probable" indicates circumstantial evidence exists linking the pesticide to the episode's effects.

3/ In all cases 1 human received medical attention.

APPENDIX E

REPORT EPISODES OF BURNS SUFFERED FROM THE APPLICATION OF CREOSOTE AS AN HERBICIDE (Adapted from PERS, 1976)[1]

Date of Episode	State	Causative Agent Verification[2]	Remarks[3]
4/21/73	CA	Probable	A pest control operator sustained chemical burns of the face while spraying weeds.
6/14/73	CA	Probable	A lumber company worker was spraying weeds. Wind blew the herbicide into his face and the worker sustained first degree burns.

---

[1] Records checked from 1967 through April, 1976.

[2] Verification indicates whether the pesticide associated with the episode was established as the causative agent which resulted in death, illness, etc. "Yes" indicates that substantial evidence exists linking the pesticide to the episode's effects; "Probable" indicates circumstantial evidence exists linking the pesticide to the episode's effects.

[3] In all cases 1 human received medical attention.

REFERENCES

1. American Wood Preservers' Association (1976). AWPA Book of Standards, Washington, D.C.

2. American Wood Preservers' Institute, Environmental Programs Task Group Subcommittee No. 5 (1977). "Creosote and Creosote Solutions-Wood Preservatives." Memorandum for the Office of Pesticide Programs, Environmental Protection Agency.

3. Berenblum, I. and R. Schoental (1947). "Carcinogenic Constituents of Coal-Tar." British Journal of Cancer 1:157-165.

4. Birdwood, G.T. (1938). "Keratitis from Working with Creosote." British Medical Journal 2:18.

5. Bonser, Georgiana M. and M.D. Manch (1932). "Tumors of the Skin Produced by Blast-Furnace Tar." Lancet I:775-776.

6. Boutwell, R.K. and D.K. Bosch (1958). "The Carcinogenicity of Creosote Oil: Its Role in the Induction of Skin Tumors in Mice." Cancer Research 18(10):1171-1175.

7. Bramhall, G. and P.A. Cooper (1972). "Quality Comparison of Current Marine Piling with 25- and 40-Year-Service Piling." American Wood Preservers' Association 68:194-202.

8. Cabot, S., N. Shear and M.J. Shear (1940). "Studies in Carcinogenesis. XI. Development of Tumors in Mice Painted with 3,4 Benzpyrene and Creosote Oil Fractions." American Journal of Pathology 16: 301-312.

9. "Carcinogen Assessment Group's Report on Coal Tars" (1978). Office of Research and Development, Environmental Protection Agency.

10. "Carcinogen Assessment Group's Report on Creosote" (1977). Office of Research and Development, Environmental Protection Agency.

11. Committee on Biologic Effects of Atmospheric Pollutants, National Research Council (1972). Biologic Effects of Atmospheric Pollutants, Particulate Polycyclic Organic Matter. Washington, D.C.: National Academy of Sciences.

12. Cookson, H.A. (1924). "Epithelioma of the Skin After Prolonged Exposure to Creosote." British Medical Journal 68(1):368.

13. Cummings, Willard (1977). Use Profile for Coal Tar Derivatives (Exclusive of Wood Preservatives). Unpublished EPA Report.

14. Davies, J.I. and W.C. Evans (1964). "Oxidative Metabolism of Naphthalene by Soil Pseudomonads. The Ring-Fission Mechanism." Biochemistry Journal 91:251-261.

15. Dean-Raymond, D. and Rutgers R. Bartha (1975). "Biodegradation of Some Polynuclear Aromatic Petroleum Components by Marine Bacteria." Technical Report No. 5; Research Sponsored by the Office of Naval Research Under Contract N0014-67-A-0115-0005, Task Number NR 137-843.

16. Deelman, H.T. (1962). "Induction and Other Problems of Tar Cancer." In International Conference on the Morphological Precursors of Cancer 1962. Edited by L. Sevari, pp. 69-73.

17. Drisko, R.W. and T.B. O'Neill (1966). "Microbiological Metabolism of Creosote." Forest Products Journal 16(7):31-34.

18. Dunn, Bruce P. and Hans F. Stich (1975). "The Use of Mussels in Estimating Benzo[a]pyrene Contamination of the Marine Environment (38971)." Proceedings of the Society for Experimental Biology and Medicine 150:49-51.

19. Dunn, Bruce P. and Hans F. Stich (1976a). "Monitoring Procedures for Chemical Carcinogens in Coastal Waters." Journal of the Fisheries Research Board of Canada. 33(9):2040-2046.

20. Dunn, Bruce P. and Hans F. Stich (1976b). "Release of the Carcinogen Benzo[a]pyrene from Environmentally Contaminated Mussels." Bulletin of Environmental Contamination and Toxicology, 15(4): 398-401.

21. Freudenthal, Ralph and Peter W. Jones, Editors (1976). Carcinogenesis-A Comprehensive Survey. Volume 1: Polynuclear Aromatic Hydrocarbons:Chemistry, Metabolism, and Carcinogenesis. New York, Raven Press.

22. Fuller, B., R. Holberger, D. Carstea, J. Cross, R. Berman, and P. Walker (1977). " The Analysis of Existing Wood Preserving Techniques and Possible Alternatives." MITRE Technical Report 7520; METREK Division/ The Mitre Corporation. Contract No. 68-01-4310, Project No. 15060 for the Environmental Protection Agency.

23. Gibb, Herman (1978a). Phone conversation of April 25, 1978 with J.D. MacEwen (University of California) on test results of monkeys and rabbits in MacEwen et al. study.

24. Gibb, Herman (1978b). Phone conversation of May 8, 1978 with David Groth (NIOSH-Cincinati) on test results of rabbits and monkeys from MacEwen (1976) study.

25. Gibb, Herman (1978c). Phone conversation of May 5, 1978 with David Webb (AWPI) on use of coal tar-creosote AWPA Specification P1 and P2.

26. Gorski, J. (1959). "Experimental Investigations on the Carcinogenic Properties of Some Pitches and Tars Manufactured from Silesian Pit Coal." Medycyna Pracy 10(5):309-317.

27. Hanlon, G. (1938). "Creosote Poisoning of Cattle." Australian Veterinary Journal 14:73.

28. Harrison, D.L. (1959). "The Toxicity of Wood Preservatives to Stock. Part 2: Coal Tar Creosote." New Zealand Veterinary Journal 7:89-98.

29. Hawley, Gessner G. (1977). The Condensed Chemical Dictionary - New York: Van Nostrand Reinhold Company, pp. 214,237.

30. Henry, S.A. (1947). "Occupational Cutaneous Cancer Attributable to Certain Chemicals in Industry." British Medical Bulletin 4:398-401.

31. Hepner, R.D. (1977). "Investigations on the Leaching of Creosote and Creosote Degradation Products from Soil:Sand:Creosote Mixtures." Pittsburgh: Koppers Company, Inc.

32. Hochman, Harry (1967). "Creosoted Wood in a Marine Environment - A Summary Report." American Wood Preservers' Association 16:138-149.

33. Horton, W.A. (1961). "An Investigation of the Carcinogenic Properties of Various Coal Tars of Commercial Fractions Thereof." Report of the Kettering Laboratory, Department of Preventive Medicine and Industrial Health. Cincinnati: University of Cincinnati, 32 pages.

34. Horton, A. Welsey, Russell Tye, and Klaus L. Stemmer (1963). "Experimental Carcinogenesis of the Lung. Inhalation of Gaseous Formaldehyde or an Aerosol of Coal Tar by C3H Mice." Journal of the National Cancer Institute 30(1):31-43.

35. Hueper, W. and W.W. Payne (1960). "Carcinogenic Studies on Petroleum Asphalt, Cooling Oil, and Coal Tar." Archives of Pathology 70:372-384.

36. International Agency for Research on Cancer Monographs on the Evaluation of Carcinogenic Risk of the Chemical to Man: Certain Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds; Vol. 3 (1973). Lyon: International Agency for Research on Cancer.

37. Jonas, Adolph D. (1943). "Creosote Burns." Journal of Industrial Hygiene and Toxicology 25:418-420.

38. Kelso, William C. Jr. and Eldon A. Behr (1977). "Depletion of Preservatives from Round Southern Pine in Fresh Water." American Wood Preservers' Association preprint prepared for the Annual Meeting, April 1977.

39. Kennaway, E.L. (1925). "Experiments on Cancer-Producing Substances." British Medical Journal 69(2):3366-3371.

40. Kinkead, Edwin R. (1973). "Toxicity of Coal Tar Aerosol." In the Proceedings of the 4th Annual Conference on Environmental Toxicology; Paper No. 13, pp. 177-188.

41. Lander, G.D. (1926). "Veterinary Toxicology." London: Bailliere, Tindall and Cox. (Cited in Hanlon, 1938 and Harrison, 1959).

42. Leach, C.W. and J.R. Weinert (1976). "Migration of Creosote Through Pressure Treated Wood." A Report to the Environmental Program Task Group, Sub-Group No.5 (Creosote) of the American Wood Preservers' Institute.

43. Lenson, Norman (1956). "Multiple Cutaneous Carcinoma After Creosote Exposure." New England Journal of Medicine 254:520-523.

44. Lijinsky, W., U. Saffiotti and P. Shubik (1956). "A Study of the Chemical Constitution and Carcinogenic Action of Creosote Oil." Journal of the National Cancer Institute 18:687-692.

45. Lijinsky, W., I. Donsky, G. Mason, H.Y. Ramahi, and T. Safovi (1963). The chromatographic determination of trace amounts of polynuclear hydrocarbons in petroleum mineral oil and coal tar. Analyt. Chem. 35: 952.

46. Lorenz, L.F. and L.R. Gjovik (1972). Analyzing creosote by gas chromatography: Relationship to creosote specifications. Proceedings AWPA. 68:32-42 (Cited in American Wood Preservers'Institute, 1977).

47. Luke, D. (1954). "Liver Dystrophy Associated with Coal Tar Pitch Poisoning in the Pig." Veterinary Record 66(43):643-645.

48. MacEwen, James D., Allen Hall III, and Lester D. Scheel (1976). "Experimental Oncogenesis in Rats and Mice Exposed to Coal Tar Aerosols." AMRL Technical Report No. 76-125 In the Proceedings of the Seventh Annual Conference on Environmental Toxicology.

49. MacEwen, J.D. and E.H. Vernot. Toxic Hazards Research Unit Annual Technical Report: 1972, 1973, 1974, 1975, 1976. Ohio: Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base.

50. Mackenzie, S. (1898). "Yellow Pigmentary Stains of Haemorrhagic Origin" and "A Case of Tar Eruption." British Journal of Dermatology 10:417.

51. Mauro, Vittorio (1951). "Precancerous Skin Manifestations in Workers Employed in Distilling Tar." Folio Medica 34(6):281-296.

52. McConnell, Ernest E. and David H. Specht (1973). "Lesions Found in Animals Exposed to Coal Tar Aerosols." In the Proceedings of the Fourth Annual Conference on Environmental Toxicology; Paper No. 14, pp. 189-198.

53. McGaughy, R.E. (1978). EPA memo of July 25, 1978 to Herman J. Gibb. Carcinogenicity of coal tar neutral oil.

54. McMillan, B.T. (1976). "Data on Applicator Exposure." A Report to the Environmental Program Task Group, Subgroup No. 5 (Creosote) of the American Wood Preservers Institute.

55. Miller, D.J. (1977). "Loss of Creosote from Douglas-Fir Marine Piles." Forest Products Journal 27(11):28-33.

56. Mitchell, Ann D. and Dennis T. Tajiri, 1978. "*In Vitro* Mammalian Mutagenicity Assays of Creosote P1 and P2." SRI International. Unpublished report for EPA, Contract No. 68-01-2458.

57. Mittelman, Abraham (1978). Exposure Analysis for Creosote, Coal Tar and Coal Tar Neutral Oils. (Unpublished Report).

58. National Research Council Committee (1945). "Compounds in Coal Tar Creosote." Chemistry of Coal Utilization. New York: John Wiley and Sons, Inc. pp. 1357-1370.

59. NIOSH. Criteria for a Recommended Standard...Occupational Exposure to Coal Tar Products (1977). U.S. Department of Health, Education, and Welfare, Public Health Service; Center for Disease Control; National Institute for Occupational Safety and Health, DHEW (NIOSH) Publication No. 78-107.

60. O'Donovan, W.J. (1920). "Epitheliomatous Ulceration Among Tar Workers." British Journal of Dermatology and Syphilis 32:215-252.

61. Olafson, Peter and John Leutritz,Jr. (1958). "The Toxicity of Creosote and Creosote-Pentachlorophenol Mixtures to Cattle." American Wood Preservers' Association 55:54-57.

62. Pesticide Episode Review System (1976). Report No. 61 "Summary of Reported Episodes Involving Creosote." Office of Pesticide Programs, Environmental Protection Agency. April 29, 1976.

63. Pjitzer, Emil A., Paul Gross and Marianne Kaschak (1965). "Range-finding Toxicity Tests on Creosote (64-451B)." Pittsburgh: Industrial Hygiene Foundation of America, Inc. for Koppers Company, Inc. 12 pages.

64. Poel, William E. and A.G. Kammer (1957). "Experimental Carcinogenicity of Coal-Tar Fractions: The Carcogenicity of Creosote Oils." Journal of the National Cancer Institute 18(1):41-50.

65. Roe, F.J.C., Dorothy Bosch and R.K. Boutwell (1958). "The Carcinogenicity of Creosote Oil: The Induction of Lung Tumors in Mice." Cancer Research 18:1176-1178.

66. Rosmanith, J. (1953). "A Case of Cancerous Tumor Caused by Tar Vapors in a Scar Left After Erythematous Lupus." Pracovni Lekarstvi 5: 270-272.

67. Ross, Philip (1948). "Occupational Skin Lesions due to Pitch and Tar." British Medical Journal 2:369-374.

68. Sall, Robert D. and M.J. Shear (1940). "Studies in Carcinogenesis. XII. Effect of the Basic Fraction of Creosote Oil on the Production of Tumors in Mice by Chemical Carcinogens." Journal of the National Cancer Institute 1:45-55.

69. Sasmore, Daniel P. (1976). Histopathologic Evaluation of Animal Tissues from Coal Tar Studies (Rat, Rabbit, Hamster, and Mouse). Performed under NIOSH Contract No 210-75-0050. (Unpublished Report).

70. Schipper, I.A. (1961). "The Toxicity of Wood Preservatives for Swine." American Journal of Veterinary Research 22(88):401-405.

71. Schwartz, Louis (1942). "Dermatitis- From Creosote-Treated Floors." Industrial Medicine 11(8):387.

72. Shambaugh, Philip (1935). "Tar Cancer of the Lip in Fishermen." Journal of the American Medical Association 104:2326-2329.

73. Shabad, L.M., A.B. Linnik, V.P. Tumanov and L.S. Rubetskoy (1971). "Possible Blastomogenicity of Tar-Containing Ointments." Eksperimental' naya Khiurugiya i Anesteziologiya 16(6):6-9.

74. Simmon, Vincent F. and Denis C. Poole (1978). "In Vitro Microbiological Mutagenicity Assays of Creosote P1 and Creosote P2." SRI International, for EPA, Contract # 68-01-2458.

75. Smale, B.C. 1977. "Coal Tar Creosote and Coal Tar Pesticides as Candidates for RPAR." Unpublished EPA report.

76. Smith, Templeton, (Koppers Company), 1977. Letter of August 26, 1977 to Jerome P. Flesch (Hazard Evaluation and Technical Assistance Branch, HEW). HEW Health Hazard Evaulation Determination Report.

77. Stasse, H.L. (1967). "1958 Cooperative Creosote Project: IV Marine Tests; Analysis of Marine Panels After Exposure for Six and a Half Years." In Proceedings of the American Wood Preservers' Association 63:95-105.

78. Stasse, H.L. (1964). "A Study of Creosote Treatment of Seasoned and Green Southern Pine Poles. 9. Effect of Variables on Vapor Loss and Movement of Oil." American Wood Preservers' Association 60:109-128.

79. Sweeney, T.R., T.R. Price, R.A. Saunders, Sigmund M. Miller, and F.G. Smith, Walton (1958). "Coal Tar Creosote Studies; Part 1 - A Method for the Accelerated Evaluation of Marine Wood Preservatives." 14(1):295-301.

80. Tsutsui, H. (1918). "Concerning the Artificially Induced Cancroid (Cancer) in the Mouse. Gann 12:17-21.

81. Tye, Russel and Stemmer, Klaus L. (1967). "Experimental Carcinogenesis of the Lung II. Influence of Phenols in the Production of Carcinoma." Journal of the National Cancer Institute 39:175-186.

82. U.S.D.A. (1974). Food consumption, prices, expenditures. AER #138. (Cited in Mittelman, 1978).

83. U.S. Dept. of Health, Education, and Welfare, Center for Disease Control, National Institute for Occupational Safety and Health, 1977. Health Hazard Evaluation Determination Report, No. 75 - 117-372; Cincinnati, Ohio.

84. von Rumker, Rosmarie, Edward W. Lawless, Alfred F. Meiners with Kathryn A. Lawrence, Gary L. Kelso and Freda Horay (1975). "Production, Distribution Use and Environmental Impact Potential of Selected Pesticides." For the Environmental Protection Agency, Office of Pesticide Programs; EPA 540/1-74-001.

85. Wanntorp, H. (1953). "Memorandum from the State Veterinary Medical Institute, Stockholm, Sweden, to the Director N.Z. Forest Service." (Cited in Harrison, 1959).

86. Watson, A.F. and E. Mellanby (1930). "Tar Cancer in Mice. II: The Condition of the Skin When Modified by External Treatment or Diet, as a Factor in Influencing the Cancerous Reaction." British Journal of Experimental Pathology 11:311-322.

87. Webb, David A. (AWPI) Memo of December 28, 1977 to Herman Gibb (SPRD) on Creosote Committee of AWPI Answers Questions on Creosote.

88. White, Steven T. (1975). "The Influence of Piers and Bulkheads on the Aquatic Organisms in Lake Washington." Master's Thesis, University of Washington.

89. Williams, David R. (1977). Procedure for Determination of Workers' Exposures to Coal Tar Pitch Volatiles (Known also as Polycylic Particulate Organic Matter). Report of Koppers Company, Inc., Monroeville, Pennsylvania.

90. Woodhouse, D.L. (1950). "The Carcinogenic Activity of Some Petroleum Fractions and Extracts; Comparative Results in Tests on Mice Repeated After an Interval of Eighteen Months." Journal of Hygiene 48:121-134.

91. Yamagiwa, K. and Ichikawa (1915). "The Experimental Induction of Papillomas." U. Jap. Path. Ges 5:142-148.